Open Project Plan

Health Development

INVpath

Sílvia Oliveira, Biologist, Clinical Research 2025

https://globalhealthtrainingcentre.tghn.org/community/members/658019/ silvia.oli1983@gmail.com

PROJECT

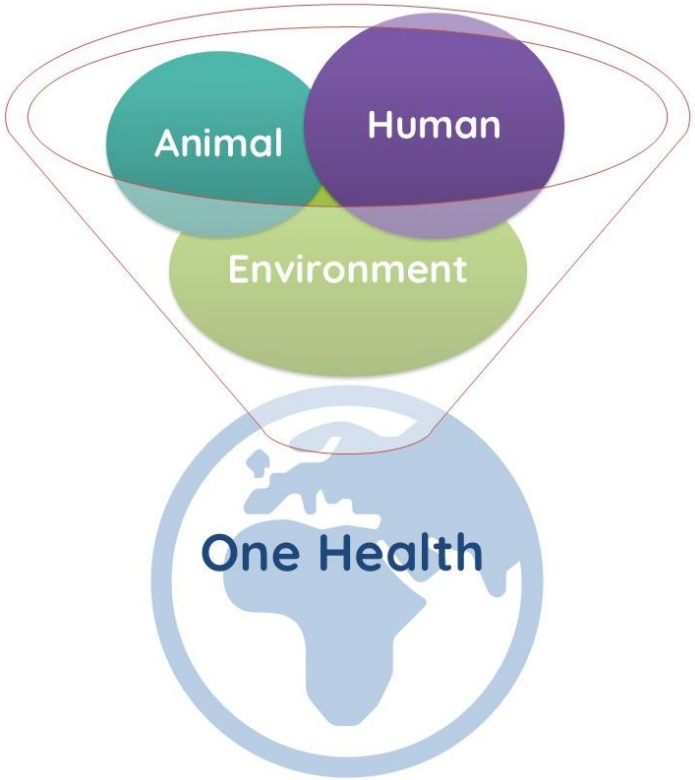
Mission

Criando Caminhos para a Investigação

Developing Paths for Research

Atividades de apoio ao Desenvolvimento e Implementação de Investigação em Saúde Humana, Animal e Ambiente, UMA SÓ SAÚDE

Activities supporting the development and implementation of research in human, animal, and environmental health, ONE HEALTH



PROJECT

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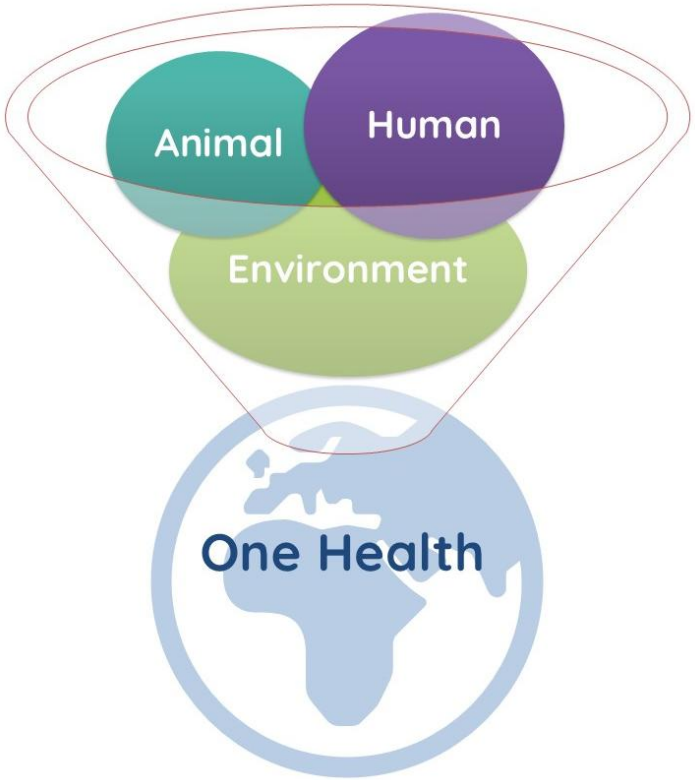
Criando Caminhos para a Investigação

Developing Paths for Research

WHO One Health is an integrated, unifying approach that aims to sustainably balance and optimize the health of people, animals and ecosystems.

“By linking humans, animals and the environment, One Health can help to address the full spectrum of disease control – from prevention to detection, preparedness, response and management – and contribute to global health security.”

https://www.who.int/health-topics/one-health#tab=tab_1



PROJECT

Mission

Criando Caminhos para a Investigação

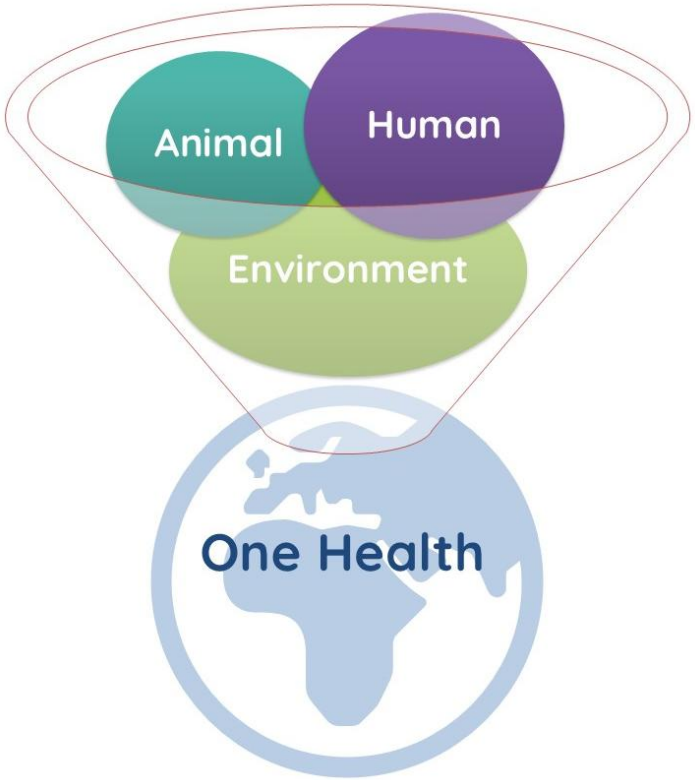
Developing Paths for Research

Human research, research conducted with or about people or their data or tissues, with the sole intention to do good.

Mandal J, Acharya S, Parija SC. Ethics in human research. Trop Parasitol. 2011 Jan;1(1):2-3. doi: 10.4103/2229-5070.72105. PMID: 23509672; PMCID: PMC3593469

Primary purpose of research involving human participants is for scientific and social value; that is, the prospect of generating the knowledge and the means necessary to protect and promote people's health.

Lancet Glob Health 2025; 13: e716–31



PROJECT

Mission

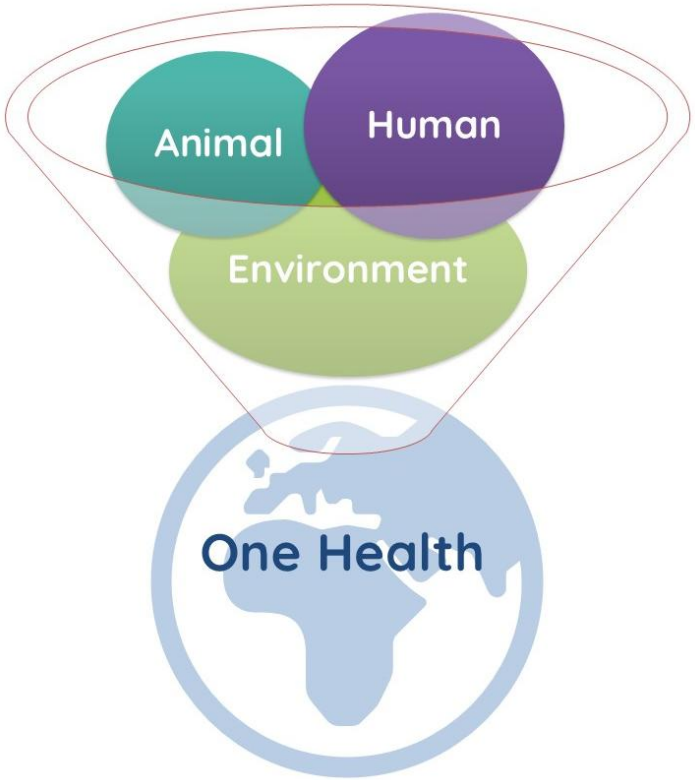
Criando Caminhos para a Investigação

Developing Paths for Research

Human Clinical Research

“Research in which people, or data or samples of tissue from people, are studied to understand health and disease. Clinical research helps find new and better ways to detect, diagnose, treat, and prevent disease. Types of clinical research include clinical trials, which test new treatments for a disease, and natural history studies, which collect health information to understand how a disease develops and progresses over time.”

https://www.cancer.gov/publications/dictionaries/cancer-terms/def/clinical-research



PROJECT

Objectives

Contribute to the development of high-quality and accessible human research, promoted by a greater diversity of stakeholders and focused on underrepresented areas — strengthening the Global Research Ecosystem across multiple dimensions, including at local and community levels.

Develop activities related to the implementation and monitoring of health research studies, aligned with WHO guidelines, regulatory agencies, ethical principles, and the 2030 Sustainable Development Goals (SDGs), centered on research participants and tailored to the specific characteristics of each population group, community, and the scientific needs of each project.

PROJECT

Values

Accessibility

Equity

Diversity

Cooperation

Compliance

Health Development INVpath

NGO/NGDO

Scientific Societies

Citizens' Organizations

Foundations

Public Entities

PROJECT

Values

Equity

Prioritize research addressing the needs of underserved populations and research teams.

Accessibility

Ensure inclusive access to research support services across all disciplines, regions, teams.

Diversity

Foster partnerships with diverse stakeholders and disciplines to enrich research outcomes and impact.

Health Development
INVpath

Collaboration

Advance open science through cross-sector collaboration and shared resources, outcomes.

Compliance

Ensure high-quality activities in accordance with applicable legislation, ethical principles, best practices.

PROJECT

Project Target Entities

Research-Promoting Entities searching for

Specialized and Accessible Research Support Services:

- ✓ Non-Governmental Organizations
- ✓ Citizen Organizations
- ✓ Scientific Societies
- ✓ Foundations
- ✓ Public/Governmental Entities

Clinical Areas

PROJECT

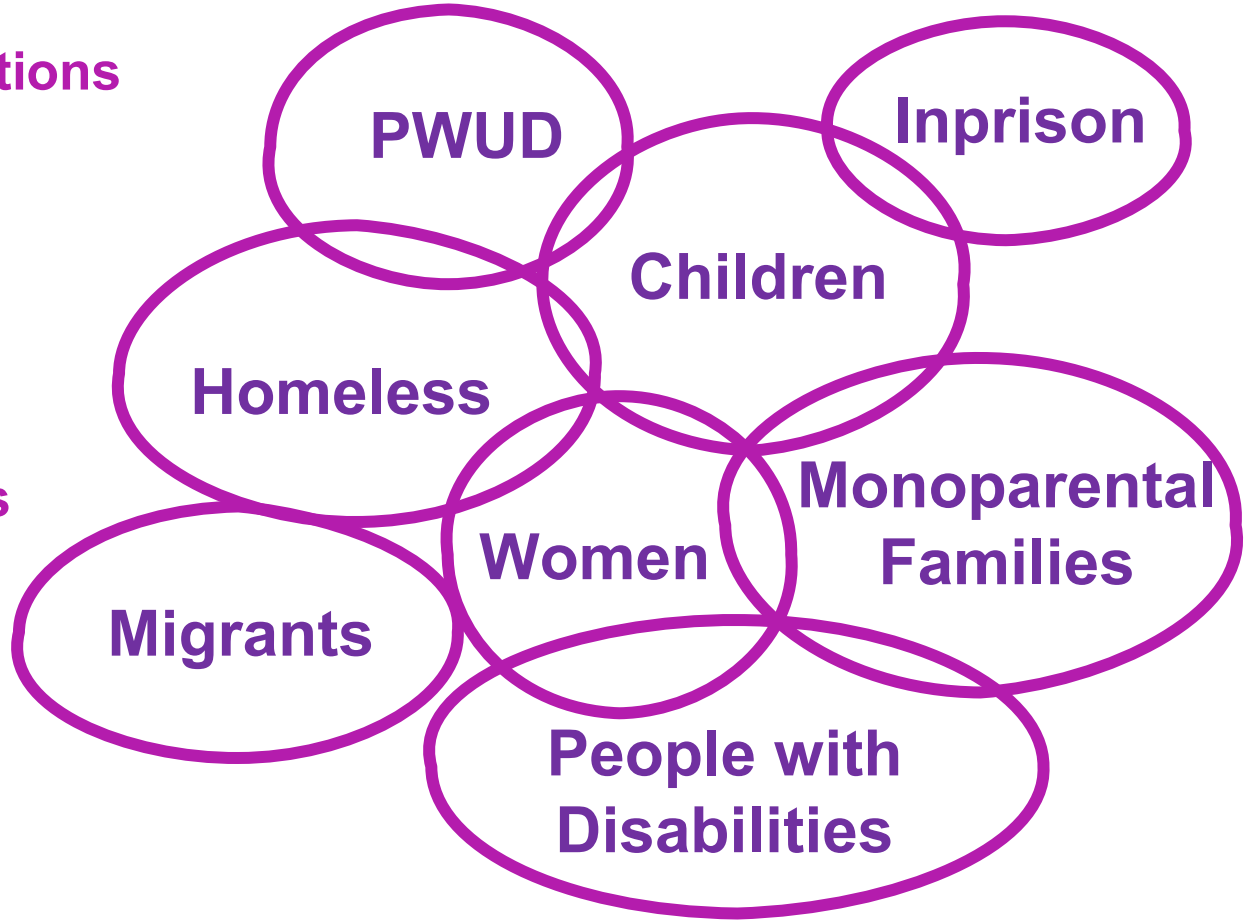
Project Target Entities

Research-Promoting Entities searching for

Specialized and Accessible Research Support Services:

- ✓ Non-Governmental Organizations
- ✓ Citizen Organizations
- ✓ Scientific Societies
- ✓ Foundations
- ✓ Public/Governmental Entities

Vulnerable and underrepresented population groups



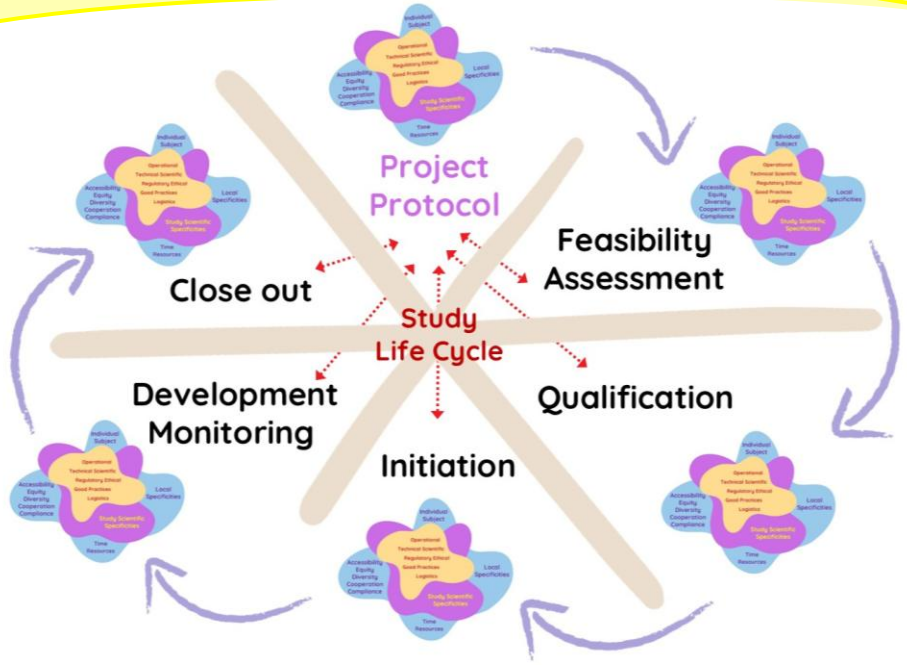
PROJECT

Activities

Human

Develop activities related to the implementation and monitoring of health research studies, aligned with WHO guidelines, regulatory agencies, ethical principles, and the 2030 Sustainable Development Goals (SDGs), centered on research participants and tailored to the specific characteristics of each population group, community, and the scientific needs of each project.

Across different stages of the Study Life Cycle



PROJECT

Definitions

Defining the Essential Elements underlaying INVpath activities Matrix within each study

PROJECT

Definitions

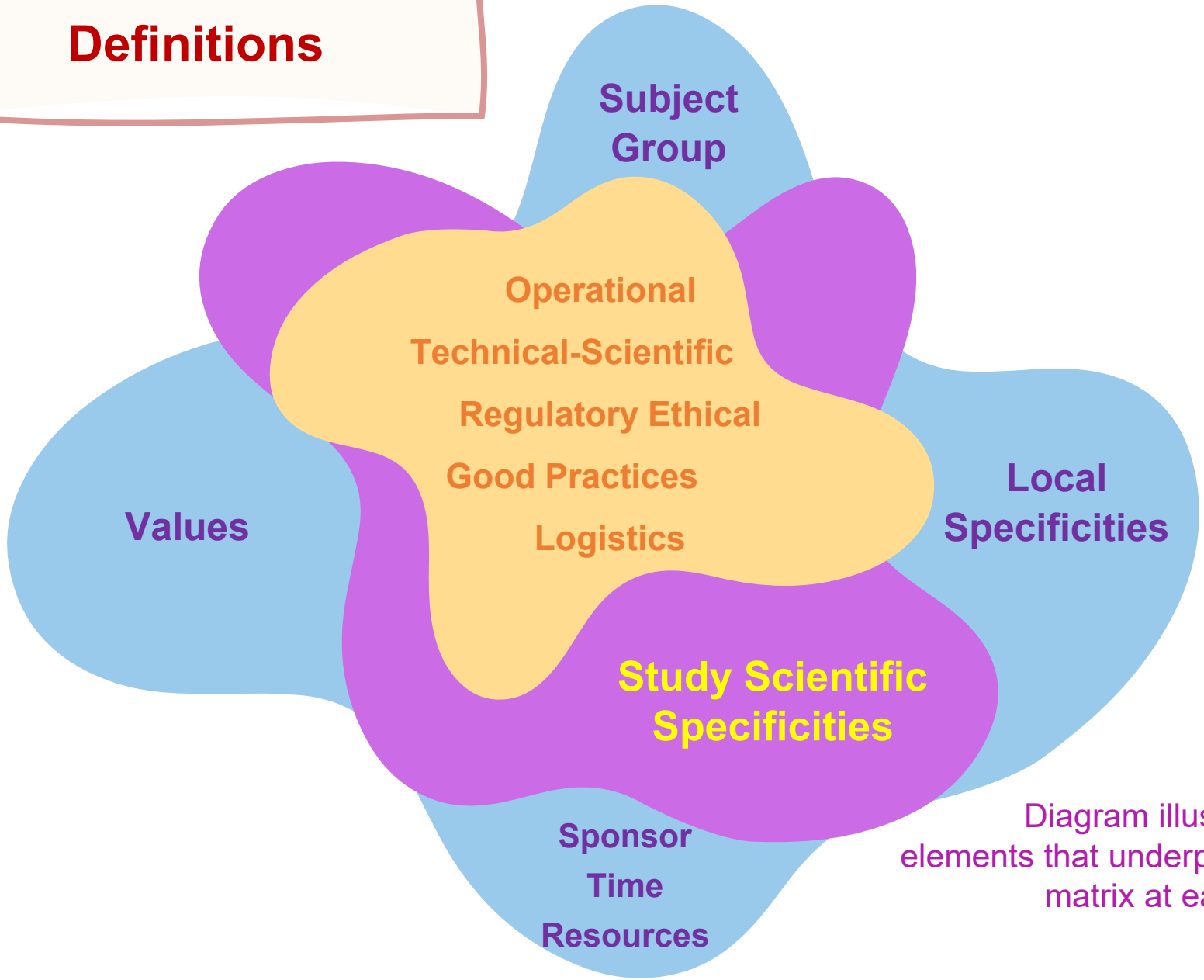
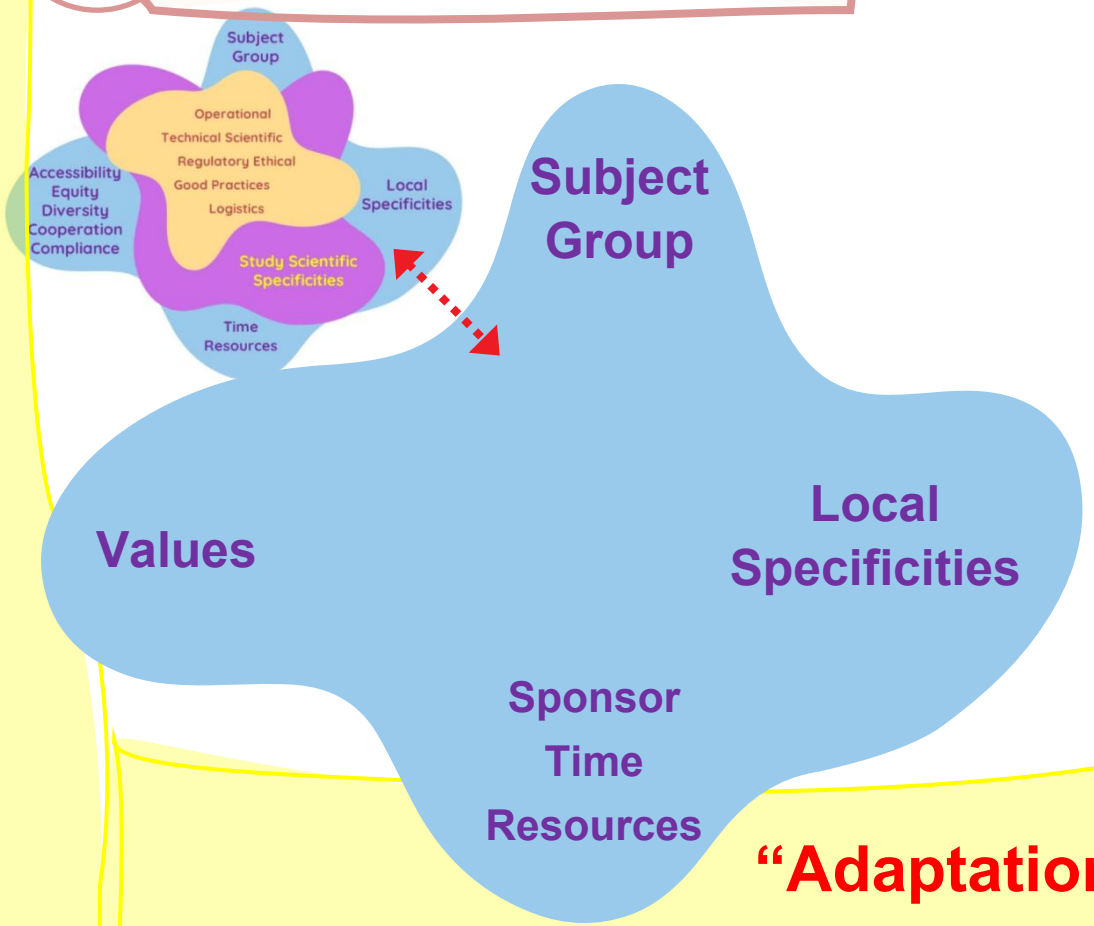


Diagram illustrating the essential elements that underpin INVpath activities matrix at each stage of a study.

PROJECT

INVpath

Definitions



Contexts of the Study

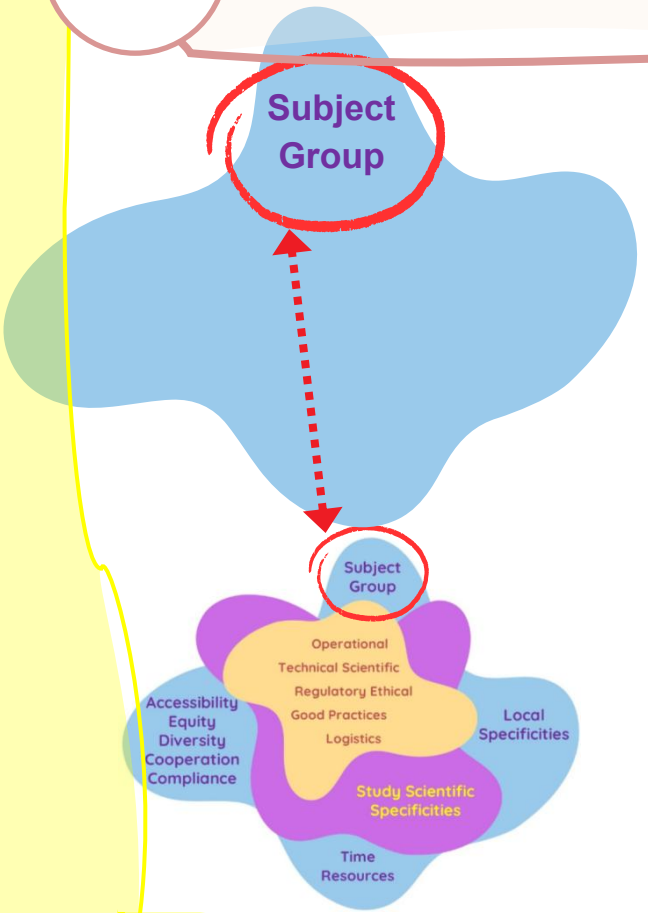
- Individual / Group / Population-level
- Location
- Values
- Resources

“Adaptation is to the experienced environment”

“Study IMPLEMENTATION” ↔ “EXISTING CONTEXT”

PROJECT

Definitions

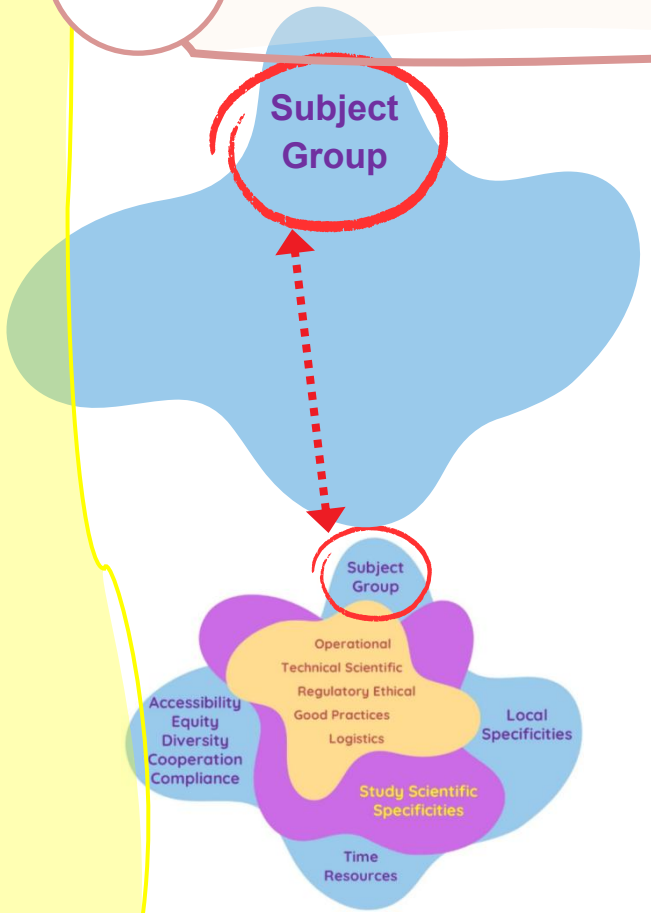


Participant Subject

- Central Element of all study activities
- Focus on Safety, Wellbeing and Rights Protection
- Part of a group and a context (Community)
- Individual uniqueness and contributor to global diversity

PROJECT

Definitions



Participant Subject

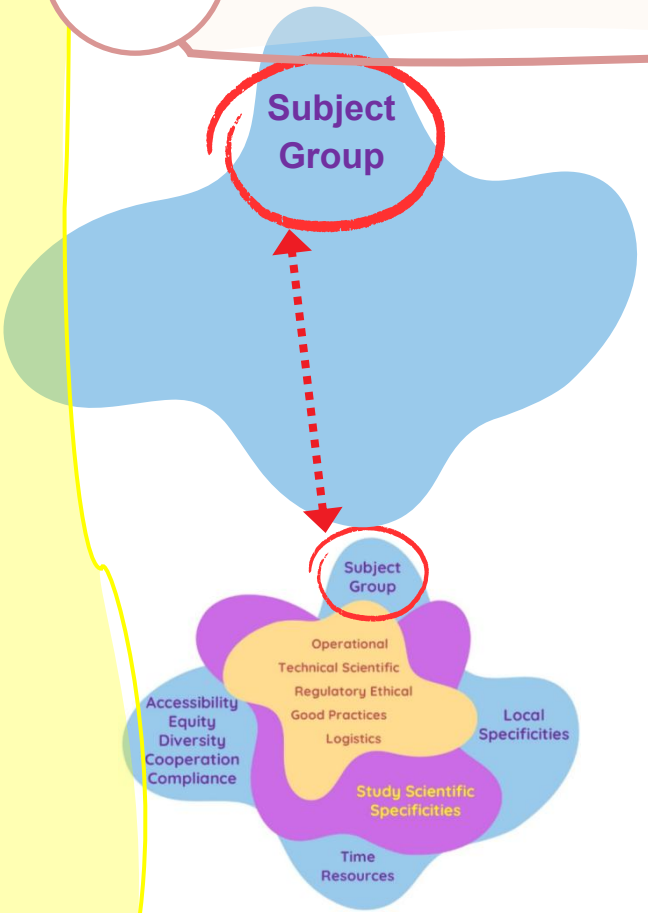
Trial Participant: An individual who participates in a clinical trial who is expected to receive the investigational product(s) or as a control. ICH E6(R3)

Principles of the Belmont Report

- ✓**Respect/Autonomy (V**oluntary ICF)
- ✓**Beneficence/Non-maleficence (Risk-Benefit**)
- ✓**Justice (F**air and non-discriminatory)

PROJECT

Definitions



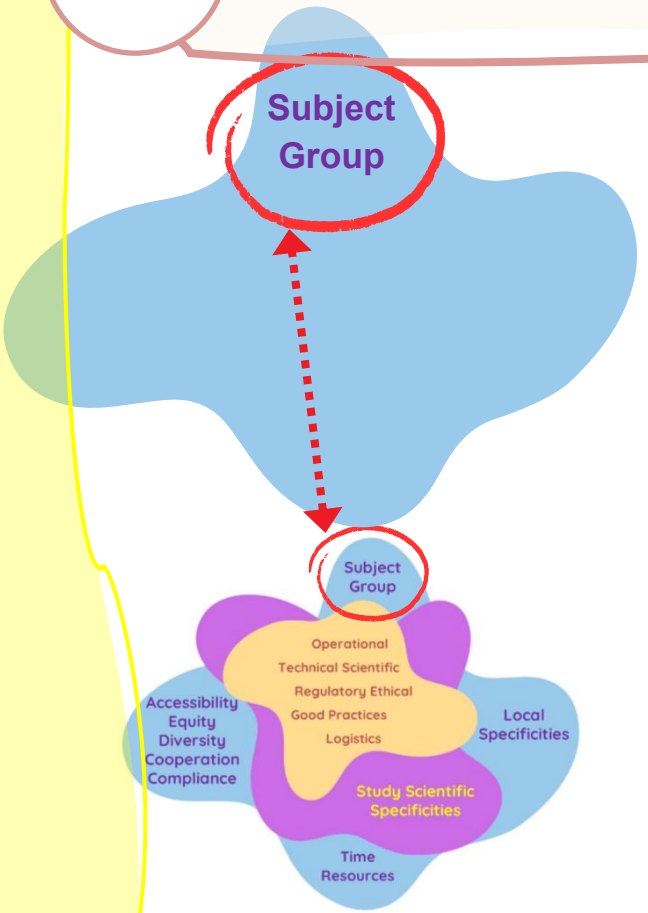
Participant Subject

Trial Participant → RIGHTS PROTECTION ICH E6(R3)

- ✓Informed Consent Form
- ✓Data Protection
- ✓Safety

PROJECT

Definitions



Use of Electronic Informed Consent in Clinical Investigations – Questions and Answers | FDA

Participant Subject

ICF Template, ICF Process, Documented Evidence:

- Template specificities per ICH-GCPs, National/Local EC (site) and legislation;
- Is there any specificities/barriers we can anticipate in the ICF consent process, related to the Patient Pop. and/or underlying disease?
- How/What are the local procedures or practices related to ICF process and its documentation requirements? Minors, reconsenting, WD, partial consenting?
- Electronic ICF process: How and where may the eIC process be conducted?

PROJECT

Definitions

Participant Subject

(21) 'Informed consent' means a subject's free and voluntary expression of his or her willingness to participate in a particular clinical trial, after having been informed of all aspects of the clinical trial that are relevant to the subject's decision to participate or, in case of minors and of incapacitated subjects, an authorisation or agreement from their legally designated representative to include them in the clinical trial;

Article 29

Informed consent

1. Informed consent shall be written, dated and signed by the person performing the interview referred to in point (c) of paragraph 2, and by the subject or, where the subject is not able to give informed consent, his or her legally designated representative after having been duly informed in accordance with paragraph 2. Where the subject is unable to write, consent may be given and recorded through appropriate alternative means in the presence of at least one impartial witness. In that case, the witness shall sign and date the informed consent document. The subject or, where the subject is not able to give informed consent, his or her legally designated representative shall be provided with a copy of the document (or the record) by which informed consent has been given. The informed consent shall be documented. Adequate time shall be given for the subject or his or her legally designated representative to consider his or her decision to participate in the clinical trial.

Regulation - 536/2014 - EN - EUR-Lex

PROJECT

Definitions

Participant Subject

GDPR and Study Participants' Rights:

- Legal wording described in the ICF related to GDPR;
- Is there a responsive and available independent ECs contact to immediately answer effectively to any questions or concerns from Participants, independent from Medical Team and Sponsor?
- Take action regarding follow up of removal of Consent at any stage of the study, including after completion?
- Access to relevant clinical information collected for study purposes, e.g. specific genetic analysis, exams, study outcomes?

Opinion 3/2019 concerning the Questions and Answers on the interplay between the Clinical Trials Regulation (CTR) and the General Data Protection regulation (GDPR) (art. 70.1.b))

Adopted on 23 January 2019

https://health.ec.europa.eu/document/download/f7be57c2-f40b-45cd-b0e9-b9d00f1234f9_en

https://www.edpb.europa.eu/our-work-tools/our-documents/opinion-art-70/opinion-32019-concerning-questions-and-answers_en

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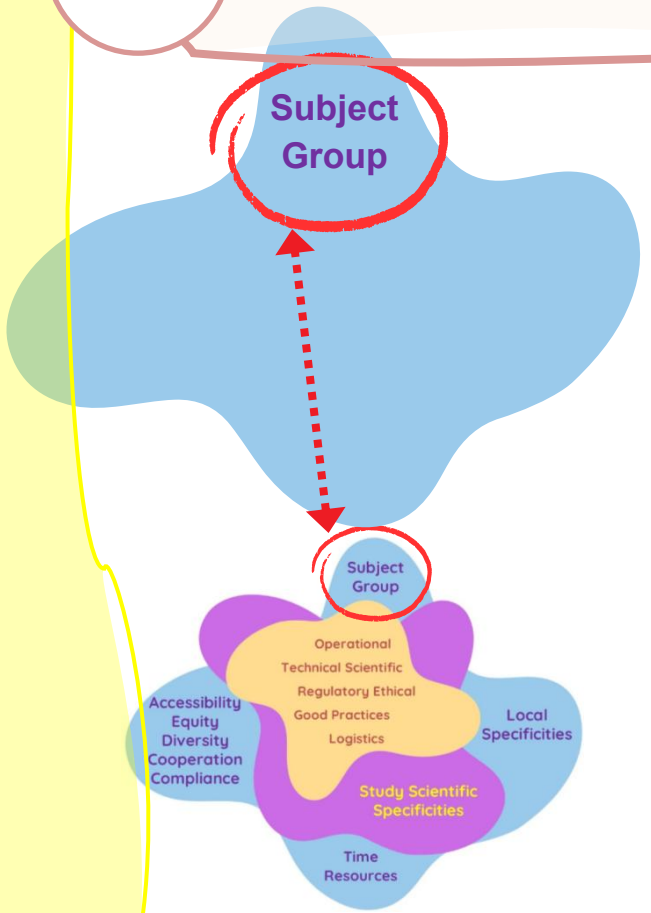
Definitions



Participant Subject

Trial Participant: An individual who participates in a clinical trial who is expected to receive the investigational product(s) or as a control. ICH E6(R3)

- Part of a group and a context (Community)
- Individual uniqueness and contributor to global diversity

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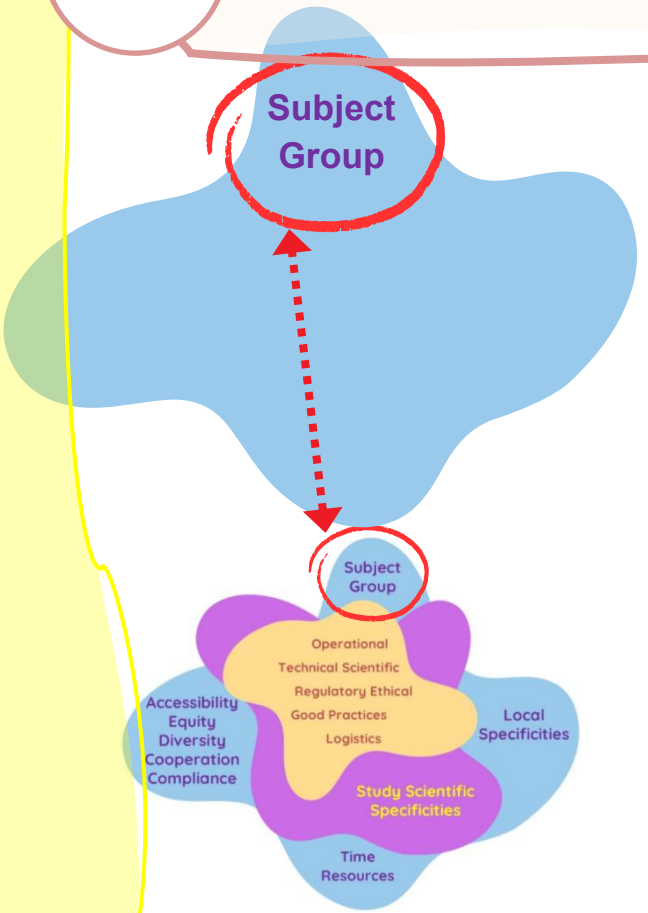
Definitions



Participant Subject

GROUP/POPULATION DIVERSITY within each study's implementation context (including ethnic factors) can influence the effects (safety and efficacy) of medicines and the risk/benefit assessment, with Potential Impact on Individuals/groups safety.

ICH E5(R1)

GUIDELINE FOR GOOD CLINICAL PRACTICE

APPENDIX A

Classification of intrinsic and extrinsic ethnic factors

INTRINSIC		EXTRINSIC
Genetic	Physiological and pathological conditions	Environmental
Gender	Age (children-elderly)	Climate Sunlight Pollution
Height Bodyweight		
	Liver Kidney Cardiovascular functions	**Culture** Socioeconomic factors Educational status Language
ADME Receptor sensitivity		
Race		Medical practice Disease definition/Diagnostic Therapeutic approach Drug compliance
Genetic polymorphism of the drug metabolism		
		Smoking Alcohol
Genetic diseases	Diseases	Food habits Stress
		Regulatory practice/GCP Methodology/Endpoints

PROJECT

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Definitions

Subject Group

ICH E5(R1)

Participant Subject

GROUP/POPULATION DIVERSITY characterization Parameters

Extrinsic Ethnic Factors: associated with the environment and culture in which a person resides. Extrinsic factors tend to be less genetically and more culturally and behaviorally determined. E.g. social and cultural aspects of a region such as medical practice, diet, use of tobacco, use of alcohol, exposure to pollution and sunshine, socio-economic status, compliance with prescribed medications, and, particularly important to the reliance on studies from a different region, practices in clinical trial design and conduct.

Intrinsic Ethnic Factors: help to define and identify a sub population and may influence the ability to extrapolate clinical data between regions. Examples of intrinsic factors include genetic polymorphism, age, gender, height, weight, lean body mass, body composition, and organ dysfunction.

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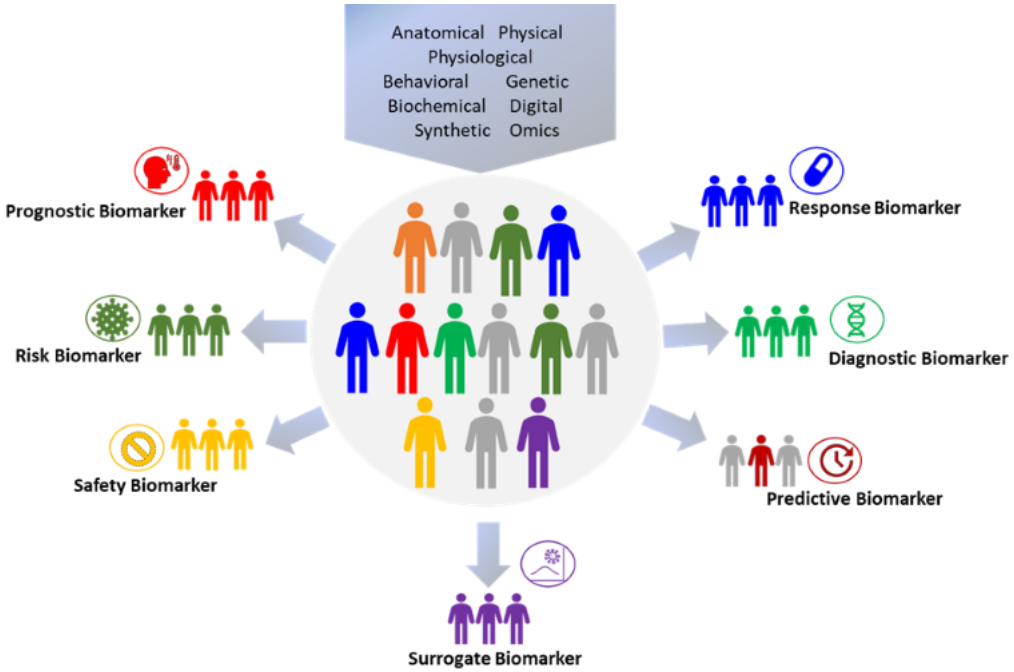
It is necessary to identify novel factors and biomarkers that, in combination, more precisely and efficiently stratify individuals into relevant subgroups, enhancing the prediction of the safety profiles of medicines and interventions.



Drug Development Through the Prism of Biomarkers: Current State and Future Outlook - AAPS Newsmagazine

Precision Medicine and Biomarkers

- ✓ Biomarkers → precision medicine to drug development by identifying specific molecular or genetic characteristics of a disease or patient population → development of more focused clinical trials, with a greater likelihood of success.
- ✓ Customized therapies → more personalized treatment approaches → better outcomes.
- ✓ Multi-omics, digital biomarkers, AI and machine learning, real world data and patient-centricity.
- ✓ Technological advances → transform how we diagnose, treat, and prevent diseases.

PROJECT

Precision Medicine and Biomarkers

OPEN ACCESS | CASE REPORTS | August 06, 2025

Multi-Regional Profiling of Epidermal Growth Factor Receptor L858R Mutation-Positive Metastatic Renal Pelvic Cancer Successfully Treated With Osimertinib

Authors: Yoshiyuki Yamamoto, MD, PhD, Atsushi Kuwahara, PhD, Atsunari Kawashima, MD, PhD, Daisuke Motooka, PhD, Yoshitake Iwamoto, MD, Takehiro Yamamoto, MD, Masako Kurashige, MD, PhD, ... SHOW ALL ... , and Norio Nonomura, MD, PhD | AUTHORS INFO & AFFILIATIONS

Publication: JCO Precision Oncology • Volume 9 • https://doi.org/10.1200/PO-25-00434

OPEN ACCESS | ORIGINAL REPORTS | August 08, 2025

Risk Score Model of Aging-Related Genes for Bladder Cancer and Its Application in Clinical Prognosis

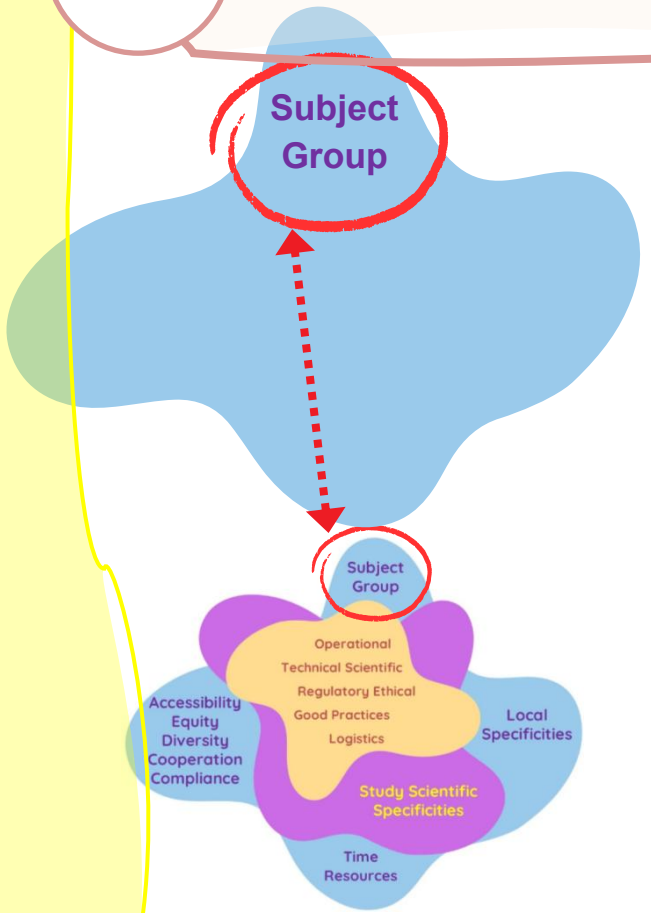
Authors: Kun Lu, MD, Liu Chao, MD, Jin Wang, MD, Xiangyu Wang, MD, Longjun Cai, MD, Jianjun Zhang, MD, and Shaoqi Zhang, MD | AUTHORS INFO & AFFILIATIONS

Publication: JCO Clinical Cancer Informatics • Volume 9 • https://doi.org/10.1200/CCI-25-00019

PROJECT

Definitions

Participant Subject



ICH E5(R1)

Considering group/population diversity at each local context (including intrinsic and extrinsic variability factors) is essential to ensure an adequate and meaningful research design and outcomes

Adequate and Well-controlled Trial

An adequate and well controlled trial has the following characteristics:

- a design that permits a valid comparison with a control to provide a quantitative assessment of treatment effect;
- the use of methods to minimize bias in the allocation of patients to treatment groups and in the measurement and assessment of response to treatment; and
- an analysis of the study results appropriate to the design to assess the effects of the treatment.

PROJECT

Definitions

Participant Subject

Home > Therapeutic Innovation & Regulatory Science > Article

Trends in the Burden for Patients Participating in Industry-Funded Clinical Trials

Analysis | Published: 08 June 2025

(2025) Cite this article

Methods

156 phase II and III protocols were analyzed.

Results

Overall burden for patients to participate in phase II and III clinical trials has been rising steadily since 2011. Procedures contributing most to participation burden include patient questionnaires, lab and blood work and routine procedures conducted at each planned visit. A notable increase in the average duration of each visit per protocol was observed in large part due to the volume of procedures performed per visit. A growing proportion of procedures contributing to participation burden are those supporting supplementary, tertiary and exploration endpoints. The results of this aggregate analysis demonstrate the value of assessing patient participation burden to inform protocol design optimization.

Trends in the Burden for Patients Participating in Industry-Funded Clinical Trials | Therapeutic Innovation & Regulatory Science

Table 4 Frequency of procedures and their proportional contribution to overall burden.

From: Trends in the Burden for Patients Participating in Industry-Funded Clinical Trials

	Mean number of procedures per protocol			Proportional contribution to burden		
	Oncology	Non-Oncology	p-value	Oncology	Non-Oncology	p-value
Medication	24.8	14.6	0.04*	14.2%	10.9%	0.06
Lab and blood tests	44.5	33.2	0.2	28.2%	25.0%	0.08
Routine exams	53.4	39.0	0.1	22.7%	19.5%	0.2
Non-invasive tests	5.0	8.5	0.2	3.7%	5.5%	0.2
Invasive Procedures	3.4	3.9	0.8	2.1%	2.0%	0.8
Imaging tests	10.8	4.1	< 0.01**	7.3%	2.1%	0.0003
Questionnaires	46.2	89.8	0.01**	20.1%	28.8%	0.06
Other	6.3	10.7	0.04	1.6%	6.2%	0.6

Note: * indicates $p < 0.05$, ** indicates $p < 0.01$, and *** indicates $p < 0.001$. Statistical comparisons between oncology protocols and non-oncology protocols were made using a t-test

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Definitions

Participant Subject

Culture, Social Determinants, Community Engagement

Article | Open access | Published: 05 September 2024

The influence of socioeconomic status on individual attitudes and experience with clinical trials

Jennifer Y. Kim, Maria Florez, Emily Botto, Xoli Belgrave, Clare Grace & Ken Getz

Communications Medicine **4**, Article number: 172 (2024) | Cite this article

Abstract

Background

Characterizing perceptions of clinical trials among the socioeconomically disadvantaged is necessary for understanding how social determinants of health such as socioeconomic disparities in education and income can affect people's awareness of and exposure to clinical trials

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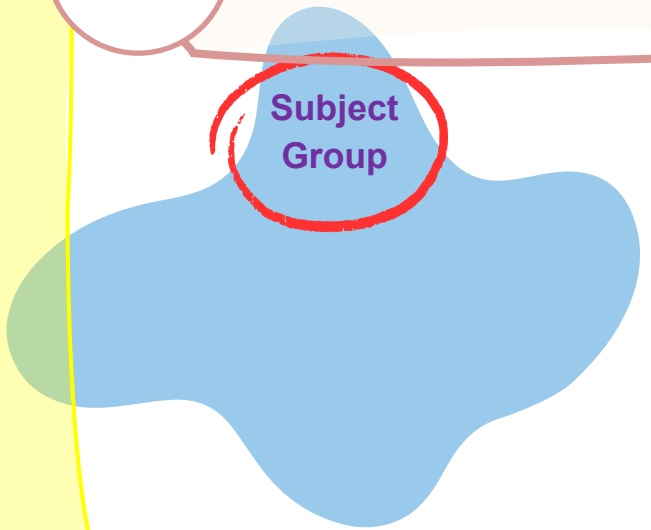
Definitions



Culture, Social Determinants, Community Engagement

Participant Subject

✓Social Determinants impacting Subject Participation, Safety and/or compliance during the study? Index tool of Protocol Equity and Selectivity could be created for protocol evaluation?

- Part of an under-served/vulnerable group or population?
- Population diversity represented in the study?
- Community engagement in the research question definition, study design and study ongoing?

✓Understand how these factors contribute to study Participant burden: recruitment, daily routine, rights, safety, health care follow up?

PROJECT

INVpath

Definitions

Subject Group

Culture, Social Determinants, Community Engagement

Participant Subject

"Some individuals, groups, and communities are in a situation of more vulnerability as research participants due to factors that may be fixed or contextual and dynamic and thus are at greater risk of being wronged or incurring harm. When such individuals, groups, and communities have distinctive health needs, their exclusion from medical research can potentially perpetuate or exacerbate their disparities. Therefore, the harms of exclusion must be considered and weighed against the harms of inclusion. In order to be fairly and responsibly included in research, they should receive specifically considered support and protections. Medical research with individuals, groups, or communities in situations of particular vulnerability is only justified if it is responsive to their health needs and priorities and the individual, group, or community stands to benefit from the resulting knowledge, practices, or interventions. Researchers should only include those in situations of particular vulnerability when the research cannot be carried out in a less vulnerable group or community, or when excluding them would perpetuate or exacerbate their disparities[3]."

ICH Good Clinical Practice E6(R3) • Global Health Training Centre

PROJECT

INVpath

Definitions

Subject Group

https://www.hra.nhs.uk/about-us/news-updates/guidance-developing-and-submitting-inclusion-and-diversity-plan-second-draft/

Participant Subject

"Key characteristics, common to several under-served groups:

- **Lower inclusion in research than one would expect from population estimates;**
- **High healthcare burden that is not matched by the volume of research designed for the group;**
- **Important differences in how a group responds to or engages with healthcare interventions compared to other groups, with research neglecting to address these factors"**

PROJECT

Definitions

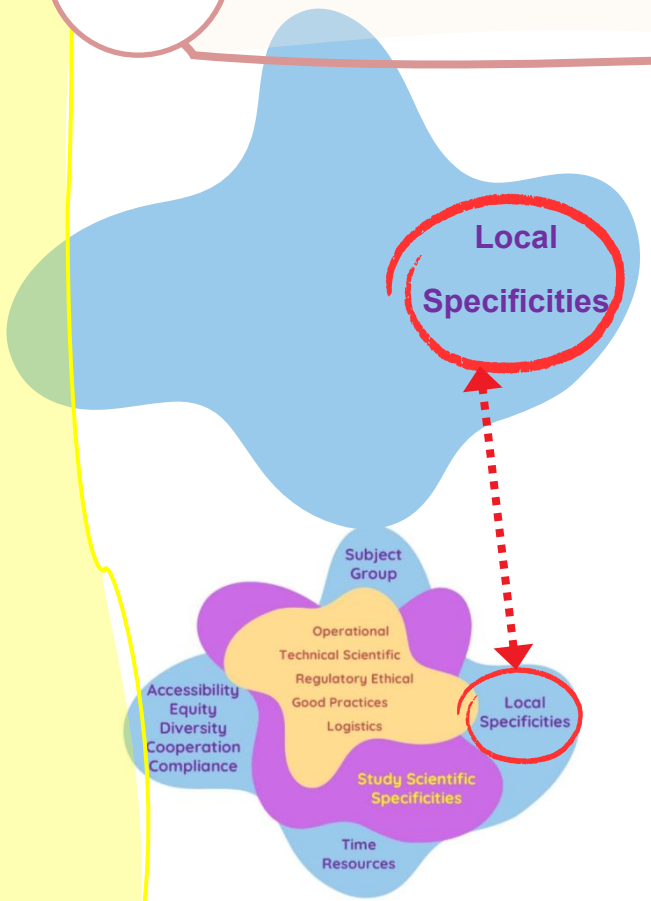
Participant Subject

Key Operational Questions linked to Social Determinants and Equity in Studies:

- How are Participants recruited/given the option to participate?
- What are the traveling requirements to comply with study procedures? Reimbursement/cost related to travel expenses, meals, work payments/days off, need to be accompanied by an additional person during the study, are limiting factors for this study? Home-Care Procedures?
- Decentralized studies: Pts self reported data (PROs), adhesion to the study procedures, role of community stakeholders and sites?
- Is there a significant change in a Participant medical follow up to participate in the study? Reference medical team change while in the study? Impact on Safety, events fup, Participant Trust/Confidence/Well being?

PROJECT

Definitions



Local Specificities

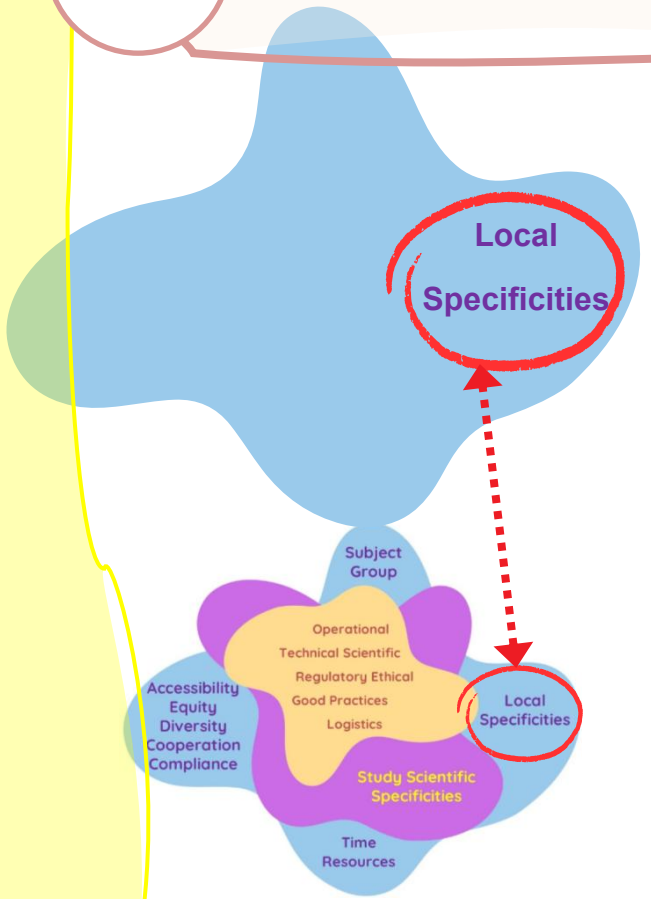
Site

Institution: Any public or private entity or agency or medical or dental organization in whose remit clinical trials are conducted. ICH E6(R3)

Investigator Site: The location(s) where trial-related activities are conducted and/or coordinated under the investigator's/institution's oversight. ICH E6(R3)

PROJECT

Definitions



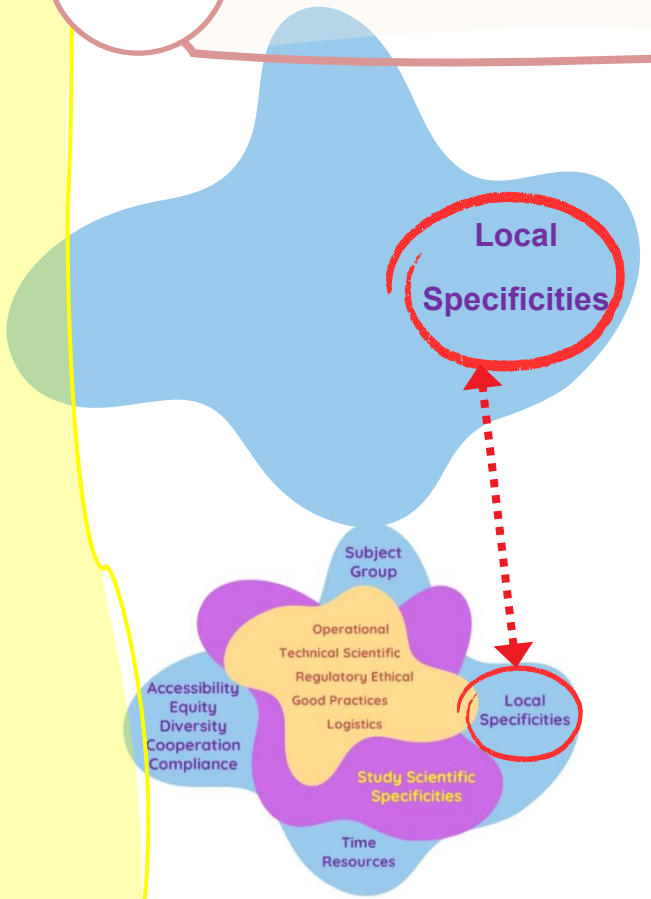
Local Specificities

Site Team

<u>Investigator:</u> A person responsible for the conduct of the clinical trial, including the trial participants for whom that person has responsibility during the conduct of the trial. If a trial is conducted by a team of individuals, the investigator is the responsible leader of the team and may be called the principal investigator. Where an investigator/institution is referenced in this guideline, it describes expectations that may be applicable to the investigator and/or the institution in some regions. Where required by the applicable regulatory requirements, the "investigator" should be read as "investigator and/or the institution." ICH E6(R3)

PROJECT

Definitions



Local Specificities

Site Team

Sub-Investigator: Any individual member of the clinical trial team designated and under the oversight of the investigator to perform significant trial-related procedures and/or to make important trial related decisions (e.g., associates, residents, research fellows). ICH E6(R3)

Service Provider: A person or organization (commercial, academic or other) providing a service used by either the sponsor or the investigator to fulfil trial-related activities. ICH E6(R3)

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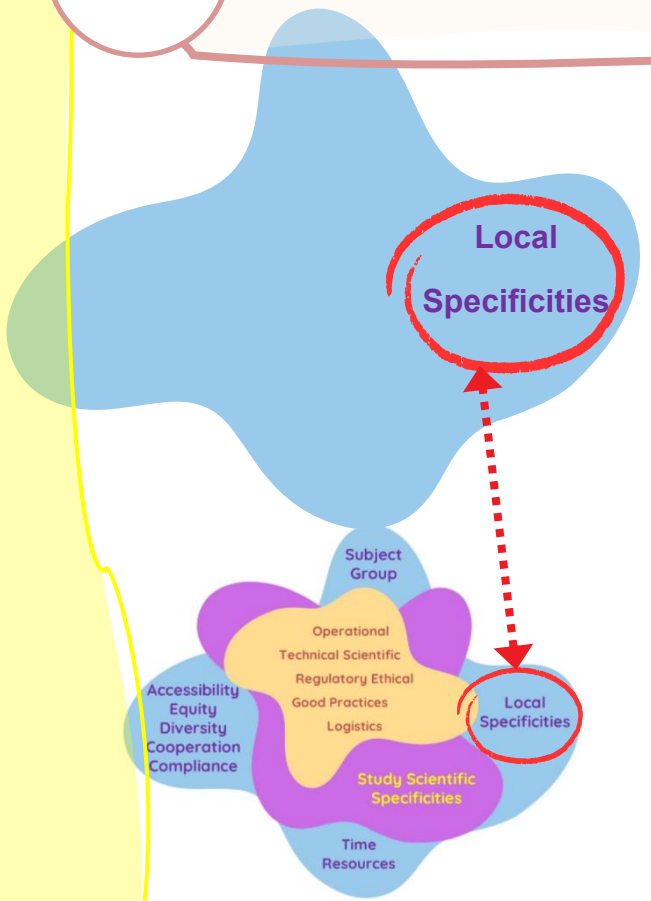
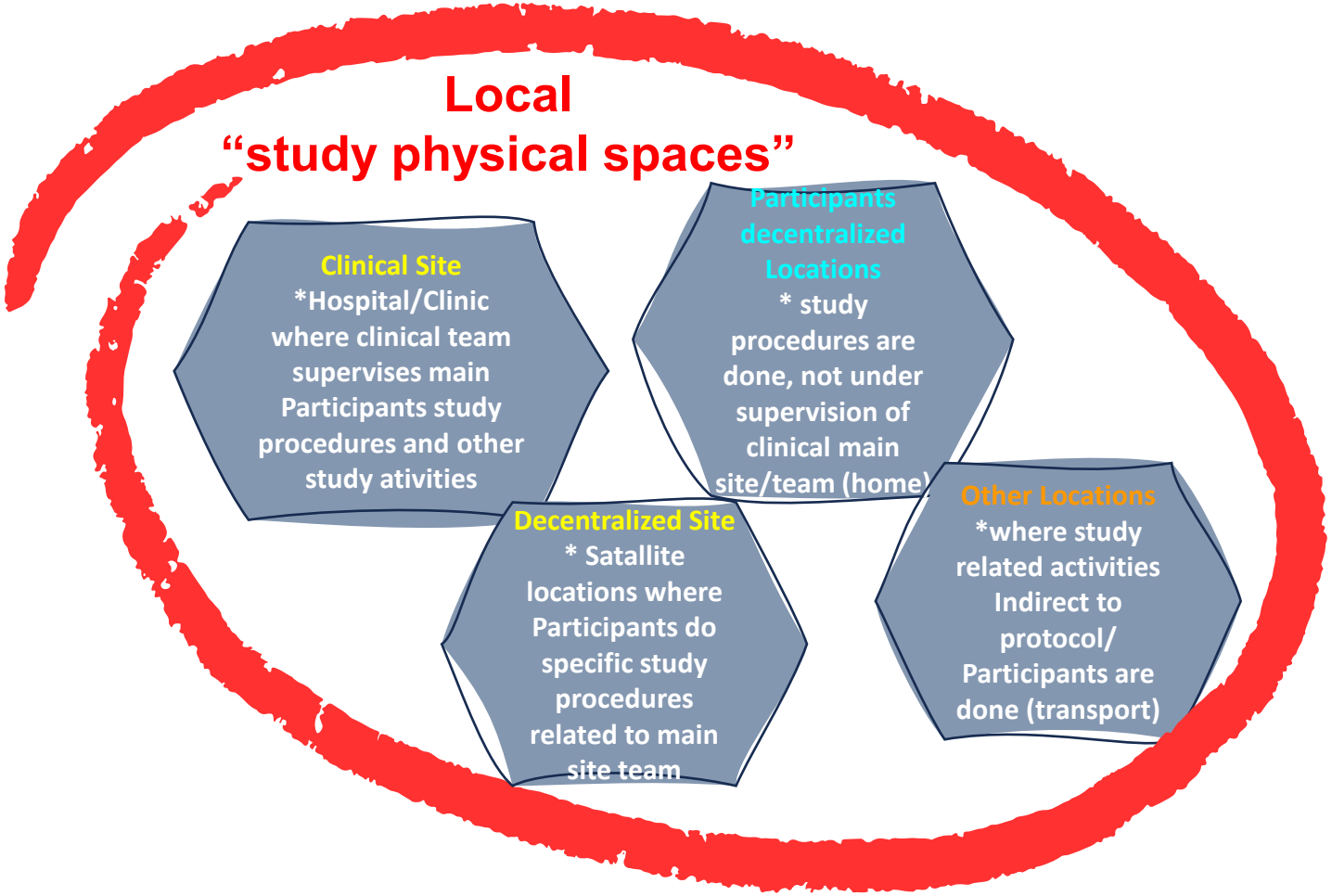
Definitions



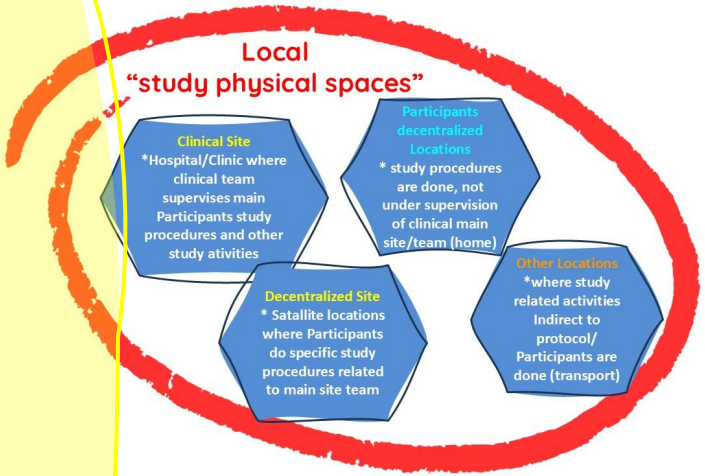
Where?

Local Specificities



PROJECT

Definitions



Where?

Local Specificities

Local Circuits:

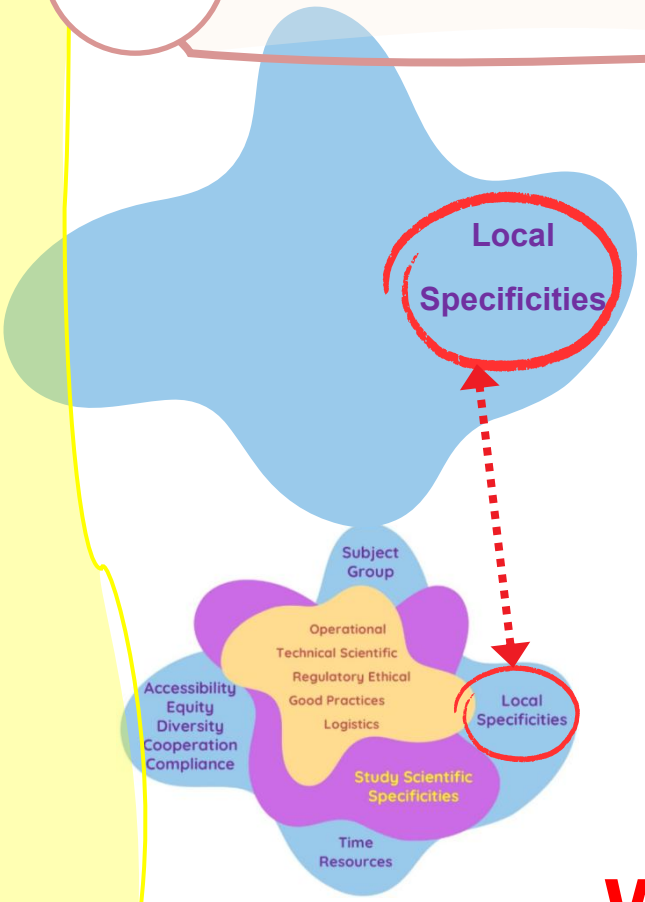
- ✓ <u>site/region/country:</u>
- Participants/Study Procedures;
- Samples;
- Data;
- Safety Reporting;
- Medication;
- Supplies (Depots, Transport, External facilities, all local "vendors)
- Equipment.

Local Equipment (study procedures and data):

- ✓ Collection of identification nr., location, Calibration certificates;
- ✓ Maintenance plan and local SOPs related to equipment used to complete study procedures and collect data;
- ✓ Acreditation and certification of facilities and local practices.

PROJECT

Definitions



Local Specificities

Who?

Local "Study Team"

Clinical Site
*Hospital/Clinic clinical team that supervises main Participants study procedures and other study ativities

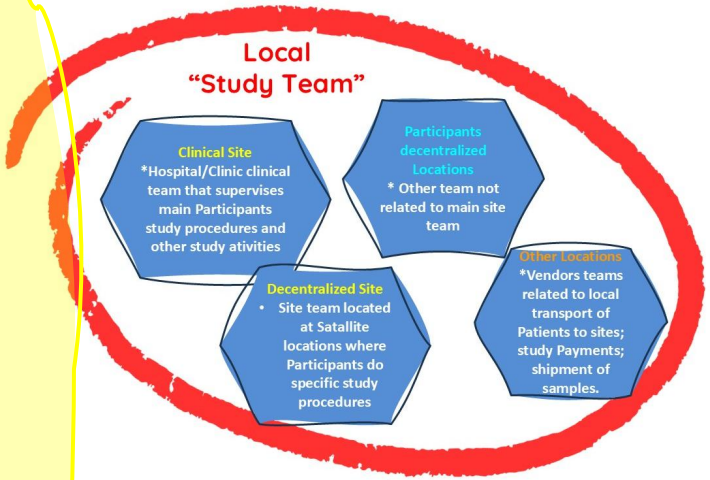
Participants decentralized Locations
* Other team not related to main site team

Decentralized Site
- Site team located at Satallite locations where Participants do specific study procedures

Other Locations
*Vendors teams related to local transport of Patients to sites; study Payments; shipment of samples.

PROJECT

Definitions



Who?

Local Specificities

Identification of persons doing study related procedures:

- Qualified, Experienced, trained and in sufficient number to complete the delegated study tasks;
- Documented evidence of timely delegation by PI;
- Essential documents provided: CV, Training docs, study contract; Delegation Log, other site docs listing study team and roles.

Identification/contacts and working hours of Site Personal, responsible for Key study procedures:

- To delivery of study supplies (pharmacy, lab, etc.)

PROJECT

Definitions

Local Specificities

Local Specificities

Local Study Teams

*Principal Investigator

*Sub-Investigator

*Nurses, Study coordinators

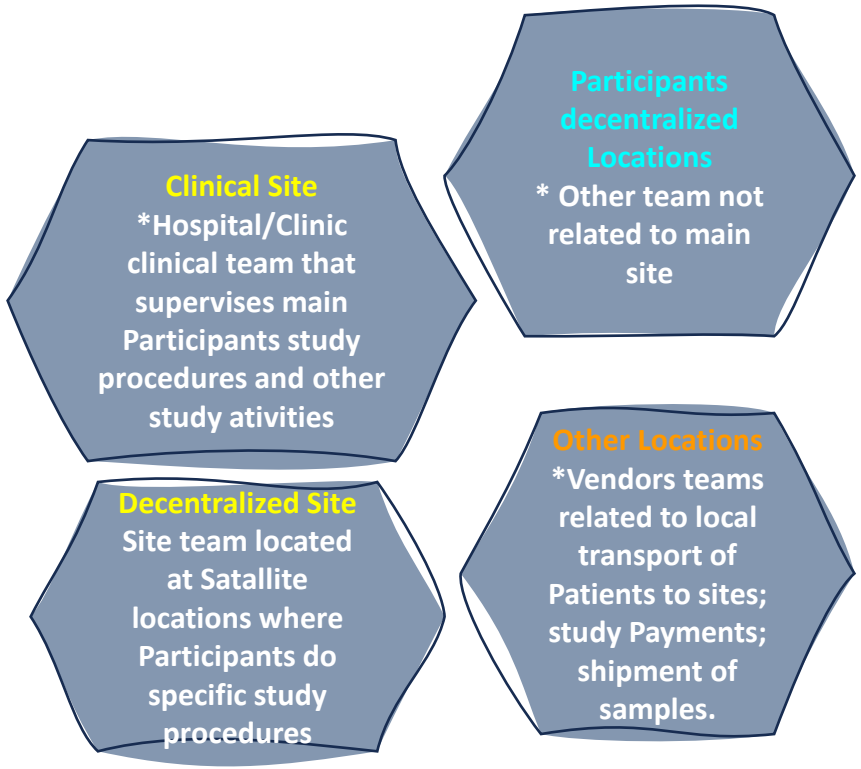
*Lab technicians

*Imaging, radiology

*ECGs

*Pharmacists

*Other (specific protocol)



*Nurses, psychologists, social, healthcare workers, peers at homecare or community-based, relevant to study, not under main site team supervision.

*Local Vendors

- Transport Pts to sites;
- Shipment of samples, meds, Pts materials from sites or Pts;
- Local PV services;
- Local Calibration/Maintenance services
- Reimbursement of Expenses to Pts

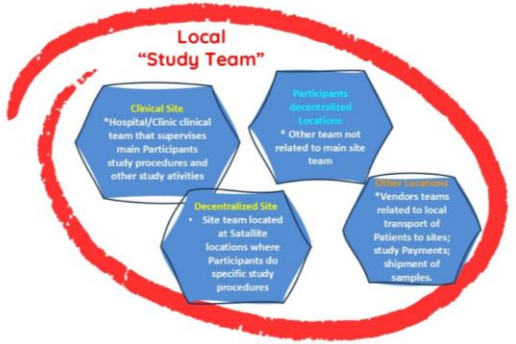
PROJECT

INVpath

Definitions

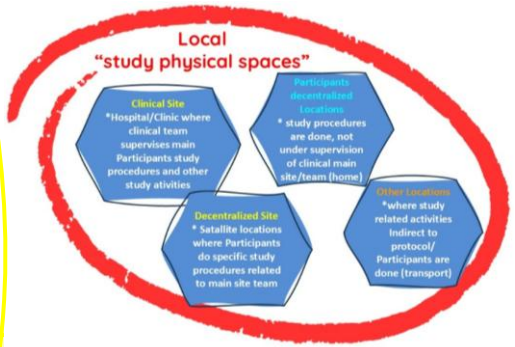
Local Specificities

Local Specificities



HOW?

- ✓ Understand and evaluate **local procedures**, quality control at local sites/providers, that impact study conduct;
- ✓ Collaborate and support sites/providers in the creation and improvement of procedures and quality control essential to study conduct **at local level**;



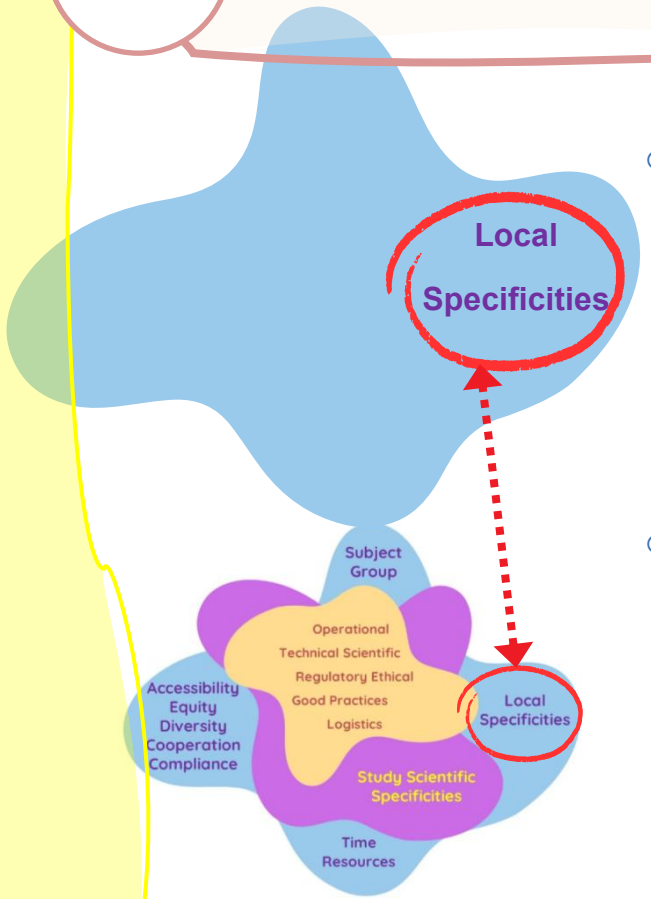
Quality Control (QC): The operational techniques and activities undertaken to verify that the requirements for quality of the trial-related activities have been fulfilled.

ICH E6(R3)

PROJECT

Definitions

Local Specificities



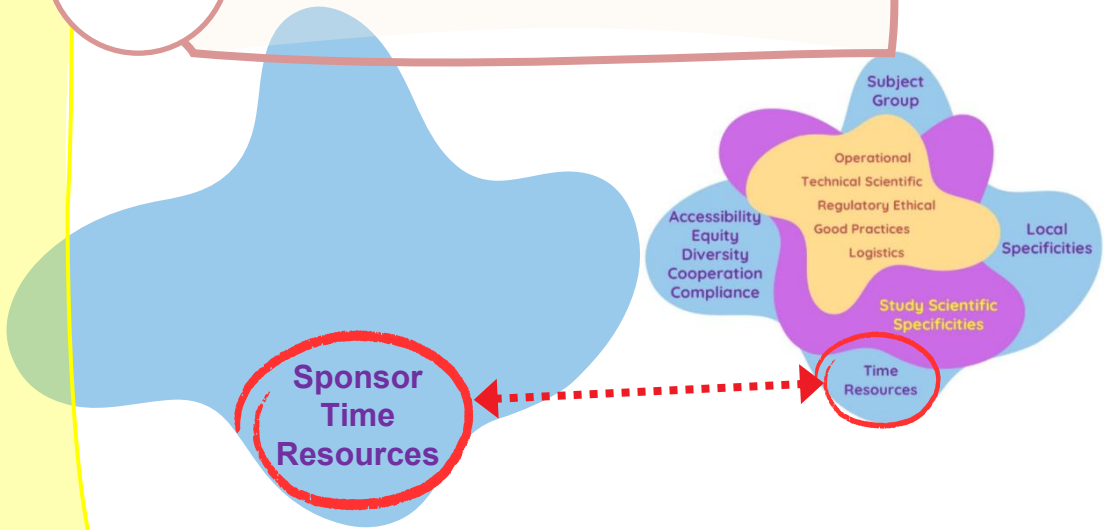
- Each site and site team is unique and different, resulting from combination of multiple local specificities: qualified human resources in sufficient number, time/availability, organization/stability, equipment/ facilities;

- Geographical locations can influence different practices within the study (e.g. climate, political stability, legislation), without invalidate protocol activities. It is essential to define the level of flexibility and adaptability of the protocol and access it, in detail, during feasibility, qualification and study development, merging it with local specificities.

Critical local factors impacting study implementation and development at each site.

PROJECT

Definitions



Sponsor-Investigator: An individual who both initiates and conducts, alone or with others, a clinical trial, and under whose immediate direction the investigational product is administered to, dispensed to or used by a participant. The term does not include any person other than an individual (e.g., the term does not include a corporation or an agency). The obligations of a sponsor-investigator include both those of a sponsor and those of na investigator.

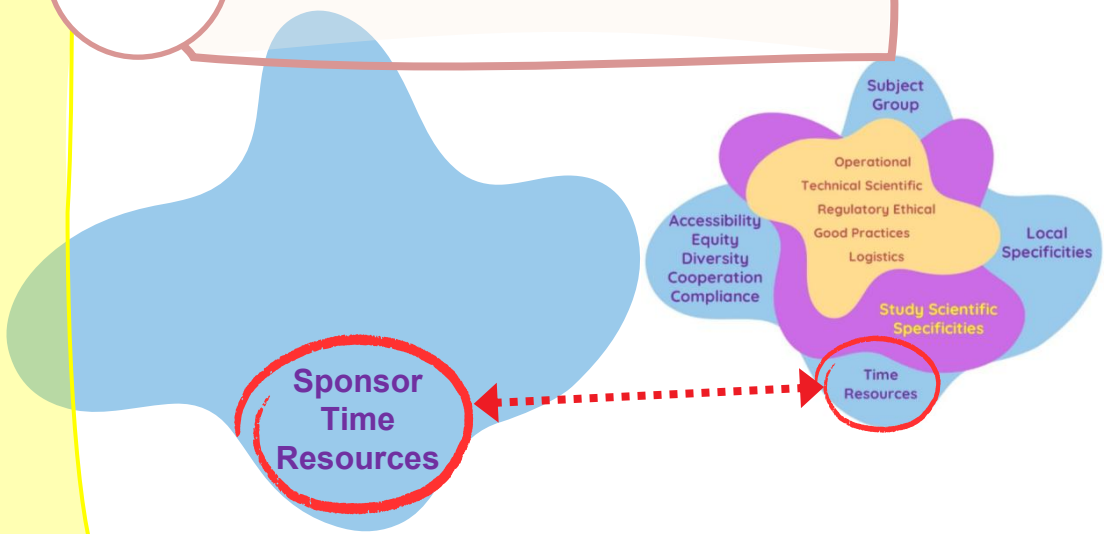
Sponsor

Sponsor: An individual, company, institution or organisation that takes responsibility for the initiation, management and arrangement of the financing of a clinical trial. A clinical trial may have one or several sponsors where permitted under regulatory requirements. All sponsors have the responsibilities of a sponsor set out in this guideline. In accordance with applicable regulatory requirements, sponsors may decide in a documented agreement setting out their respective responsibilities. Where the documented agreement does not specify to which sponsor a given responsibility is attributed, that responsibility lies with all sponsors.

ICH E6(R3)

PROJECT

Definitions



Sponsor

Home › About us › What we do › Our performance ›

Commercially and non-commercially sponsored research

Last updated on 24 Mar 2025

Research in the UK is carried out by different types of organisations that broadly fall into one of two categories – commercially or non-commercially sponsored research.

A sponsor is the organisation or partnership that takes on overall responsibility for arrangements being in place to set up, run and report a research project.

All health and social care research should have a sponsor. This includes all research that involve NHS patients, their tissue or information.

Commercially sponsored health and social care research takes place in NHS or non-NHS settings and is funded and sponsored by private sector organisations, for example pharmaceutical companies.

These studies tend to be predominantly Clinical Trials of an Investigational Medicinal Product (CTIMPs).

Non-commercially sponsored health and social care research is sponsored and funded by public bodies such as the NHS, local authorities, universities or charities.

These studies cover a much broader range of study types, including surgical, observational, diagnostic and screening studies, as well as CTIMPs.

Non-commercial studies can be funded by a commercial organisation via grants.

- ✓ All health and social care research should have a sponsor;
- ✓ Non-Commercially Sponsored Research NCSR, is funded by public bodies; local authorities, universities or charities;
- ✓ NCSR financed can by Commercial Sponsors via grants;
- ✓ Commercially Sponsored Research (Pharma Ind.)

https://www.hra.nhs.uk/about-us/what-we-do/our-performance/commercially-and-non-commercially-sponsored-research/

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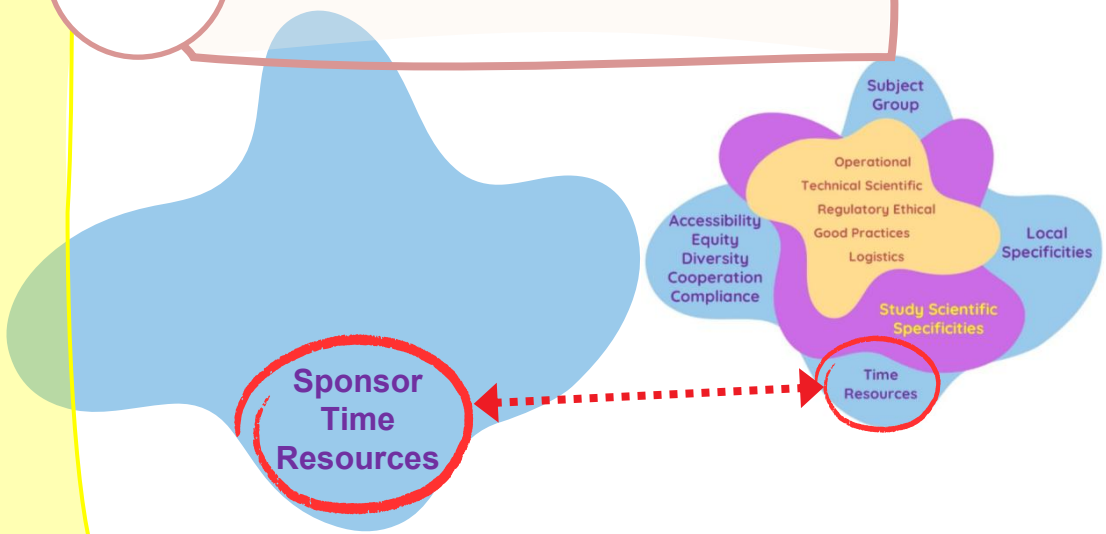
Definitions



Sponsor

Ravinetto *et al. BMC International Health and Human Rights* (2015) 15:34
DOI 10.1186/s12914-015-0073-8

BMC International Health and Human Rights

DEBATE Open Access

Sponsorship in non-commercial clinical trials: definitions, challenges and the role of Good Clinical Practices guidelines

Raffaella Ravinetto[1,2*], Katelijne De Nys[2,3], Marleen Boelaert[4], Ermias Diro[5], Graeme Meintjes[6], Yeka Adoke[7], Harry Tagbor[8] and Minne Casteels[2]

- ✓ **Single sponsor, multi-sponsors, Consortium**
- ✓ **Type of Research Study and Dimensions of the Research**
- ✓ **Specific characteristics of Non-Commercial Clinical Research, main limiting factors and difficulties (Guidelines?)**
- ✓ **Risk factors for Non-Commercial Sponsors, Studies and Participants**

https://bmcinthealthhumrights.biomedcentral.com/articles/10.1186/s12914-015-0073-8

PROJECT

Definitions

Sponsor

Home > Our work > Support for non-commercial sponsors

Support for non-commercial sponsors

The ACT EU initiative aims to **identify gaps, issues and bottlenecks** (regulatory, resourcing, operational) that prevent non-commercial sponsors from setting up and conducting clinical trials and multinational trials in particular.

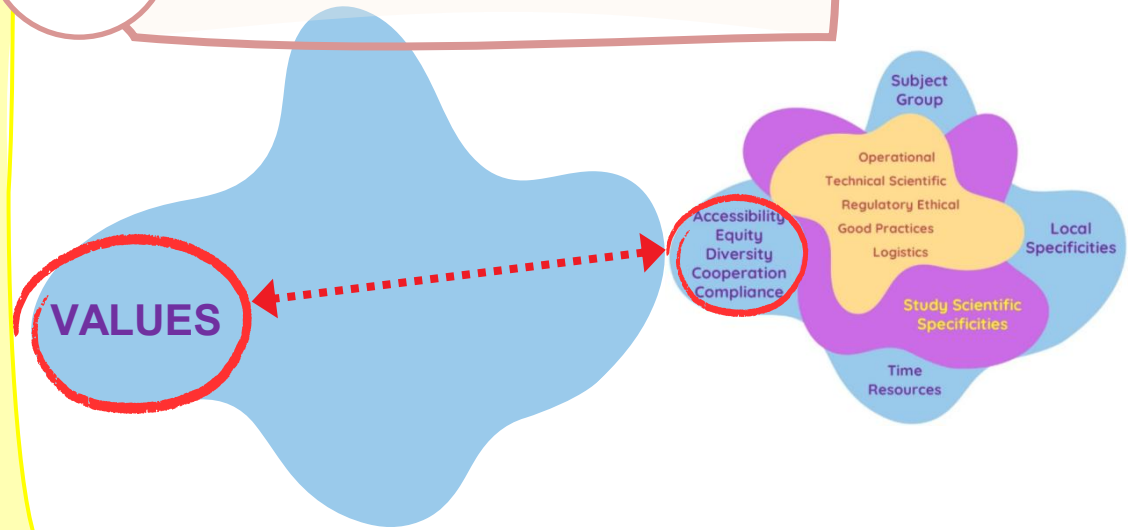
The programme intends to establish an action plan with **clear measures in place to support non-commercial sponsors** across the European Union / European Economic Area by:

- creating and maintaining a network of regulatory helpdesks, building on national activities, including extra support for questions on the Clinical Trials Regulation and the Clinical Trials Information System;
- finalising a definition of non-commercial sponsors;
- organising dedicated workshops, in liaison with the ACT EU Multi-stakeholder platform advisory group, to address prioritised topics.

https://accelerating-clinical-trials.europa.eu/our-work/support-non-commercial-sponsors_en

PROJECT

Definitions



- ✓ Purpose and Objectives of the research
- ✓ Funding and research Sponsors' goals
- ✓ Research Implementation characteristics
- ✓ Research distribution and representativeness
- ✓ Benefit of Research Outcomes

Values

Accessibility

Equity

Diversity

Cooperation

Compliance

PROJECT

INVpath

Definitions

VALUES

Values

MRC/DH/MHRA Joint Project

- **Specific Responsibilities/duties with respect to the trial:**

✓ Funder considers the scientific and financial risks

✓ Sponsor is concerned about the legal and reputational risks

✓ Healthcare organization considers the compatibility with its duty of care to patients.

- **Core set of responsibilities:**

✓ Safety of the participants and the integrity

✓ Reliability and high-quality results.

PROJECT

INVpath

Definitions

Values

AVAC
Advocacy. Access. Equity.
PrEPWatch.org HIVResourceTrack
What We Do Prevention Options

REPORT

Good Participatory Practice: Guidelines for biomedical HIV prevention trials, second edition

The Good Participatory Practice (GPP) guidelines offer trial funders, sponsors and implementers systematic guidance on how to engage stakeholders throughout the research lifecycle of HIV prevention trials.

This second edition of the guidelines, published in 2011, contains three sections: The Importance of Good Participatory Practice, Guiding Principles of GPP in Biomedical HIV Prevention Trials and Good Participatory Practices in Biomedical HIV Prevention Trials. The sections provide context, foundational principles and key practices.

[Good Participatory Practice: Guidelines for biomedical HIV prevention trials, second edition - AVAC]

1.2 What is stakeholder engagement?

Of key importance in good participatory practice is sustained, collaborative partnering with stakeholders. In the GPP guidelines, the term "stakeholder engagement" refers to processes through which trial funders, sponsors, and implementers build transparent, meaningful, collaborative, and mutually beneficial relationships with interested or affected individuals, groups of individuals, or organisations, with the ultimate goal of shaping research collectively.

Introduction

Objective of the good participatory practice (GPP) guidelines

The good participatory practice (GPP) guidelines provide trial funders, sponsors, and implementers with systematic guidance on how to effectively engage with stakeholders in the design and conduct of biomedical HIV prevention trials.

In the GPP guidelines, "design and conduct of biomedical HIV prevention trials" refers to activities required for the development, planning, implementation, and conclusion of a trial, including dissemination of trial results.

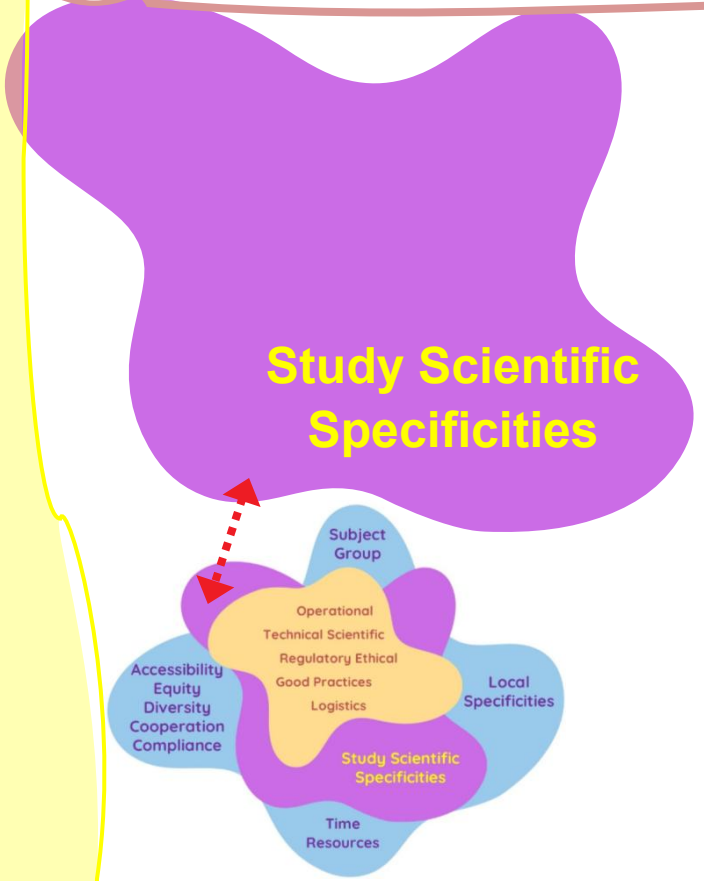
Intended audience of the GPP guidelines

The GPP guidelines are primarily written for trial funders, trial sponsors, and trial implementers. Trial funders, sponsors, and implementers include investigators, research staff, and all others involved in designing, financing, and executing biomedical HIV prevention trials. They can include governments, government-sponsored research networks, non-governmental organisations, academic institutions, foundations, public–private partnerships, and pharmaceutical or other companies.

Stakeholders not directly involved in funding, sponsoring, or implementing trials can use the guidelines to better understand the objectives, expectations, and methods of stakeholder engagement and to better evaluate such efforts.

PROJECT

Definitions



Study Scientific Specificities

- Clinical Area
- Mechanisms and dynamics of the disease and target population
- Type of study (e.g. protocol design, methodology, study phase)
- Technology used in the product, medical device or other intervention under investigation or testing

P R O J E C T

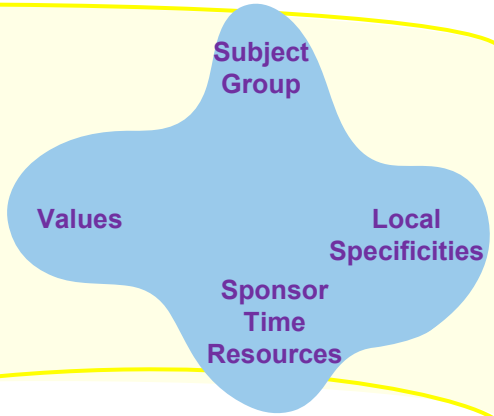
INVpath

Definitions

Study Scientific Specificities

"Adaptation is to the experienced environment"

"Study IMPLEMENTATION" ↔ "EXISTING CONTEXT"



Study Scientific Specificities

To answer a QUESTION(s) contextualized in a *"State-of-art"* of KNOWLEDGE and PROCEDURES

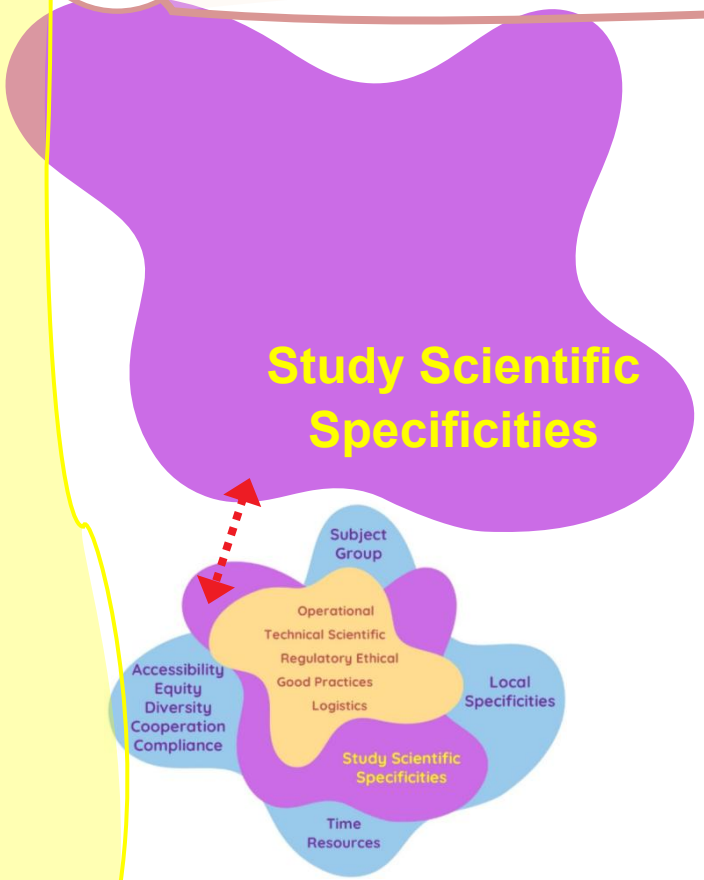
↔ aiming to GENERATE NEW VALID KNOWLEDGE about a PROCESS, part of the CONTEXT or REALITY

↔ KNOWLEDGE EVOLUTION (Real World)

PROJECT

INVpath

Definitions



Study Scientific Specificities

"Science is characterized by systematic observation and experimentation, inductive and deductive reasoning, and the formation and testing of hypotheses and theories. The details of how these are carried out can vary greatly, but these characteristics are common to all scientific activity."

https://pmc.ncbi.nlm.nih.gov/articles/PMC9710407/

PROJECT

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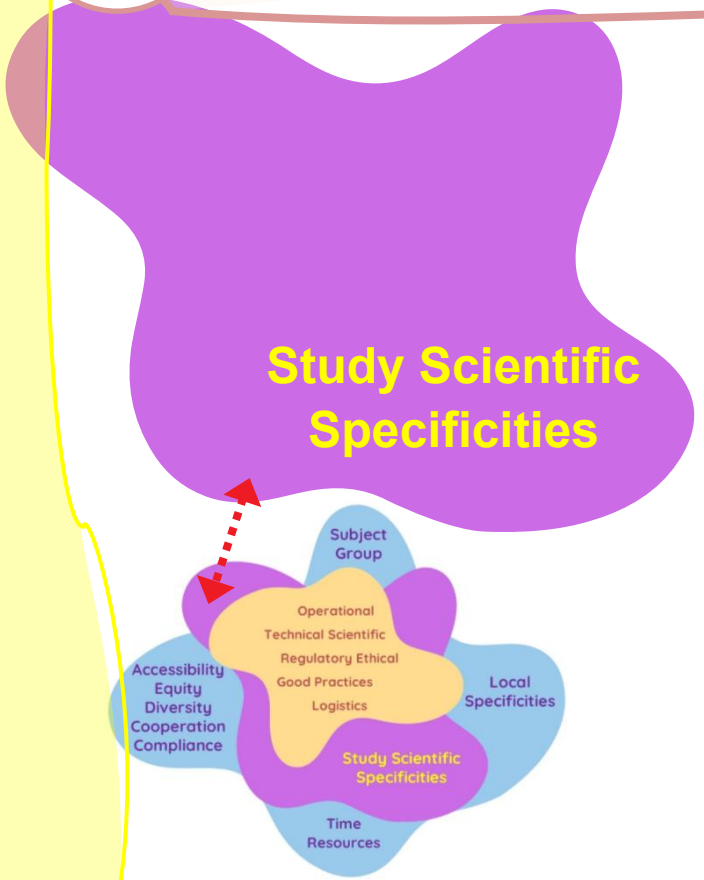
Definitions



Study Scientific Specificities

"The choice and selection of a particular methodology depends on factors such as the hypothesis to investigate, the research question or statement of the problem, the objectives, the nature of the study, the study population and controls, intervention and variables."

"Selecting an appropriate methodology is essential to obtain valid results."

https://pmc.ncbi.nlm.nih.gov/articles/PMC9710407/

PROJECT

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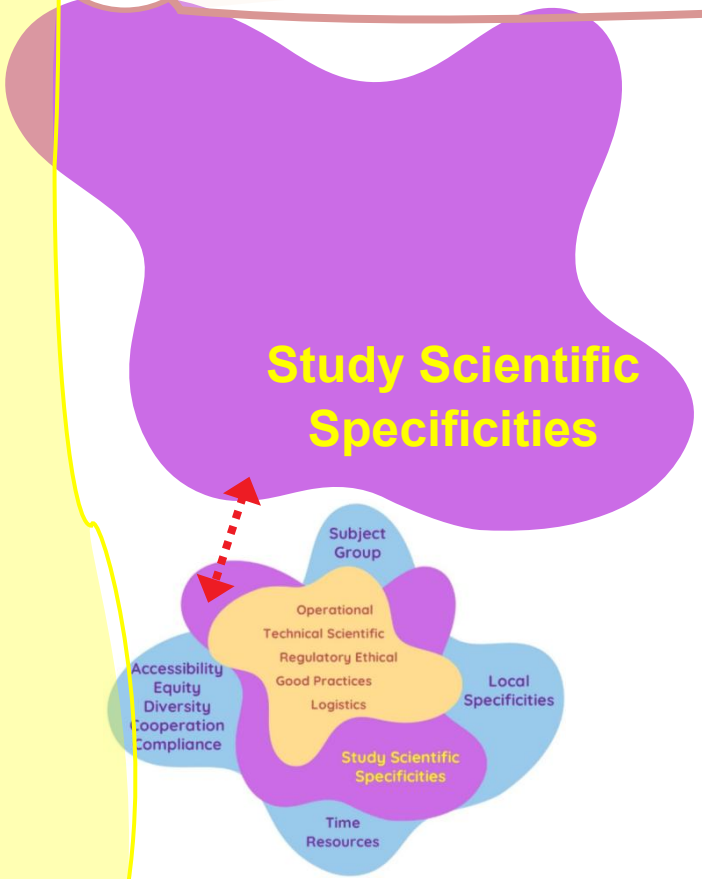
Definitions



Study Scientific Specificities

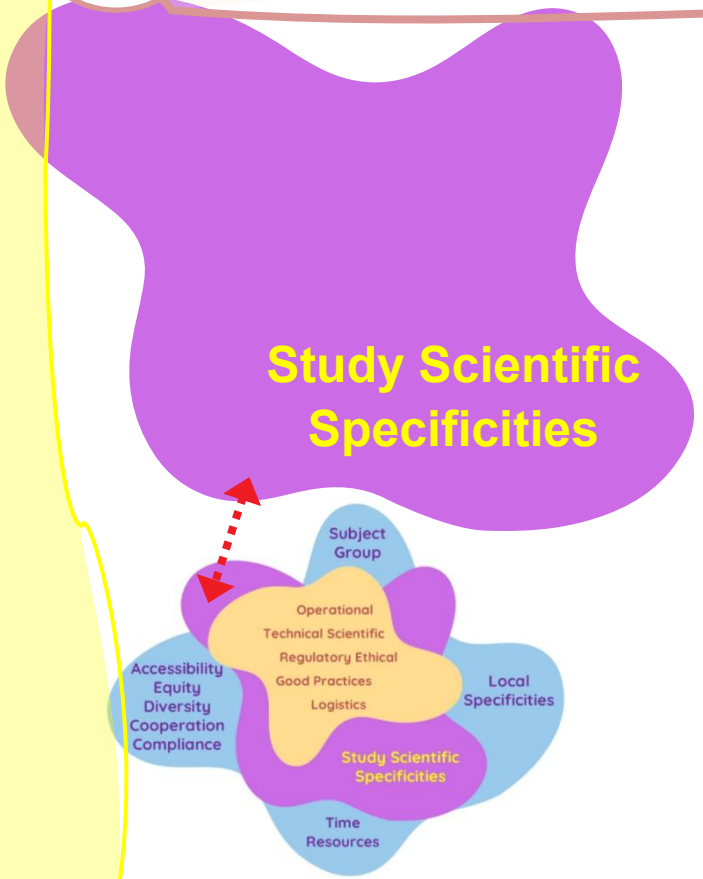
✓ **Intervention, Risk & Complexity → Key impact areas for Study Implementation (1/3)**

- **Adequate understanding of the disease, biological processes; is the Protocol design based on the most up-to-date and comprehensive scientific evidence? How is this information delivered/accessed across the different elements to ensure effective understanding?**

- **Adequate understanding of technical, specialized, and complex nature of study procedures (e.g. Biological sample handling: collection, processing, storage, shipment, and analysis; Treatment/intervention mechanisms, stability requirements, Interactions)**

PROJECT

Definitions



Study Scientific Specificities

✓ **Intervention, Risk & Complexity → Key impact areas for Study Implementation (2/3)**

- **Study Participant burden: recruitment, daily routine, rights, and safety;**
- **Impact of study complexity and duration, to its implementation at local site/teams (selection, qualification and resources management during the all stages of the study);**
- **Understand how complex assessments are translated into vendors selection and local organization (ensuring selection of quality and certified vendors) without compromising scientific key elements of the study protocol or Participants safety;**

PROJECT

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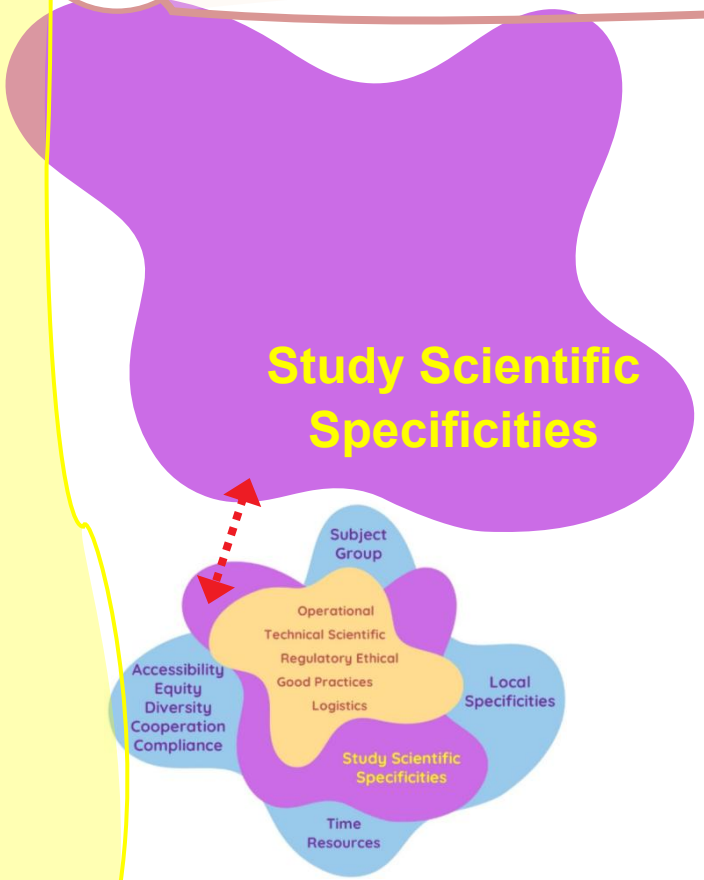
Definitions



Study Scientific Specificities

✓ **Intervention, Risk & Complexity → Key impact areas for Study Implementation (3/3)**

- **Adaptive capacity of study to integrate new information and safety data information (per EC/CA and legal requirements);**
- **Safety reporting processes and their impact on site-level management and compliance;**
- **Data collection and analysis complexity during the all stages and milestones of the study (safety).**

PROJECT

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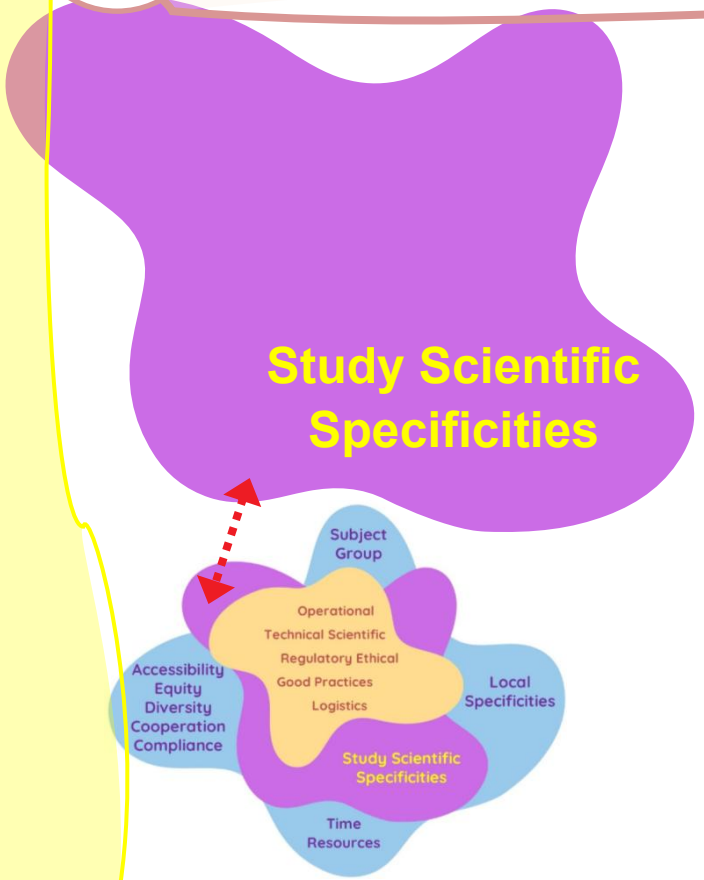
Definitions



Study Scientific Specificities

Reliability and validity of the results are dependent on:

- **The overall study design and selection of methodology: well-defined objectives, reproducible methodology, diligent data collection and analysis to minimize errors and bias, and efficient reporting of the findings.**

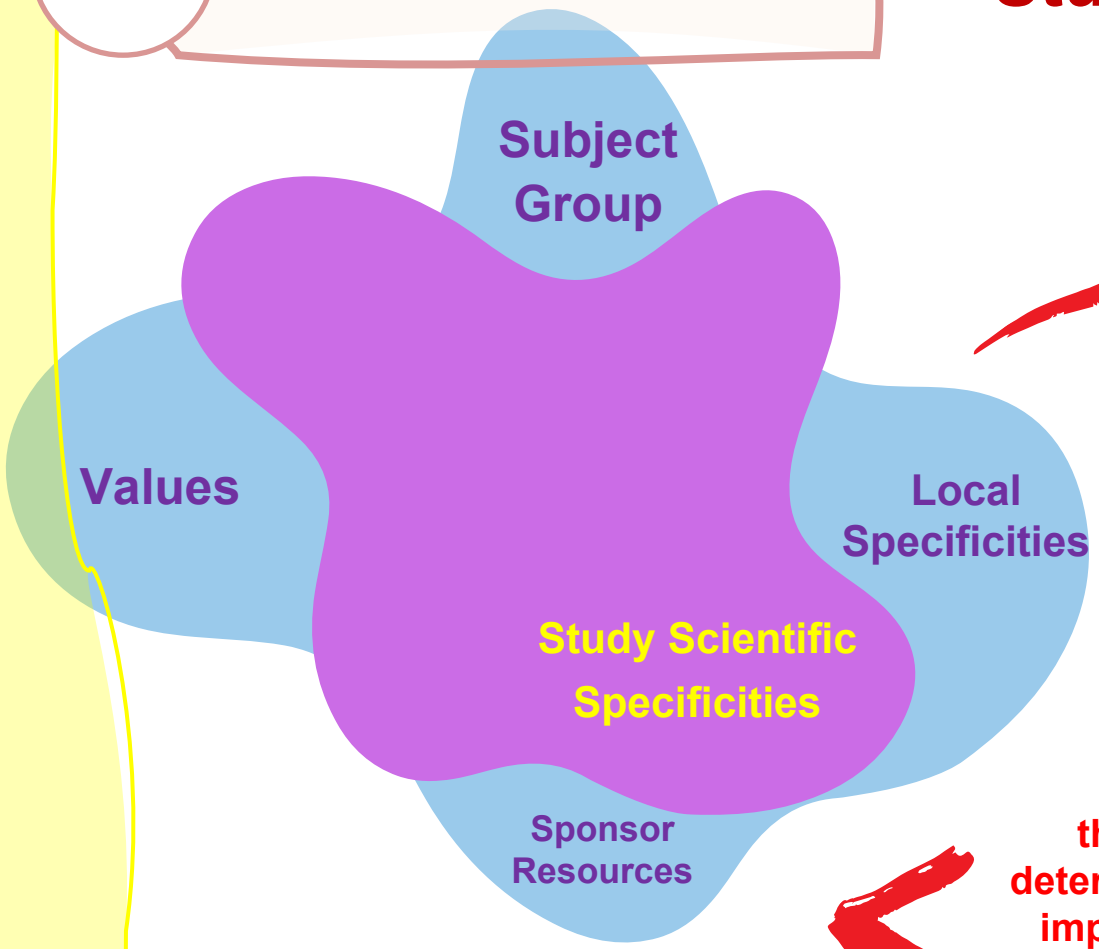
- **The understanding of the study scientific specificities, including the research methodology, to effectively, adequately translate/implement the study into practical execution.**

PROJECT

INVpath

Definitions

Study Implementation Activities



Importance of the context; Flexibility

Characterize the implementation determinants and evaluate implementation efforts.

Operational

Technical-Scientific

Regulatory Ethical

Good Practices

Logistics

Definitions

Study Implementation Activities

P
R
O
J
E
C
T

Study Scientific Specificities

"Adaptation is to the experienced environment"

"Study IMPLEMENTATION" ↔ "EXISTING CONTEXT"

Subject Group
Values
Local Specificities
Sponsor Resources

To answer a QUESTION(s) contextualized in a *"State-of-art"* of KNOWLEDGE and PROCEDURES
↔ aiming to GENERATE NEW VALID KNOWLEDGE about a PROCESS, part of the CONTEXT or REALITY
↔ KNOWLEDGE EVOLUTION (Real World)

Operational
Technical-Scientific
Regulatory Ethical
Good Practices
Logistics

The "making" of effectively translating the study protocol into reality—by applying a diverse set of rules, principles, methods, activities, and tools—so that the knowledge generated from the study is scientifically valid, reliable, and representative of the reality being investigated by the study protocol.

PROJECT

Definitions

Operational

Technical-Scientific

Regulatory Ethical

Good Practices

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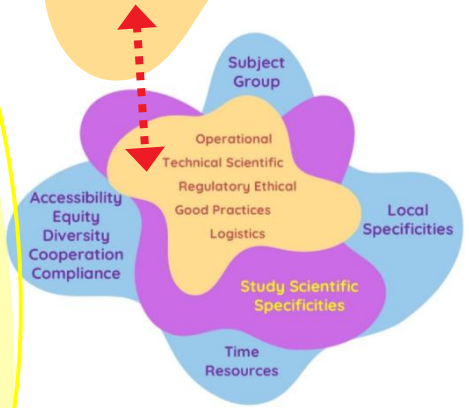

https://cancercontrol.cancer.gov/is

Study Implementation Activities

Implementation Science

field is still considered "young"

"Implementation science (IS) is the study of methods to promote the adoption and integration of evidence-based practices and interventions into routine health care and public health settings to improve our impact on population health. This discipline is characterized by a variety of research designs and methodological approaches, partnerships with key stakeholder groups (e.g., patients, providers, organizations, systems, and/or communities), and the development and testing of ways to effectively and efficiently integrate evidence-based practices and interventions into routine health settings."

PROJECT

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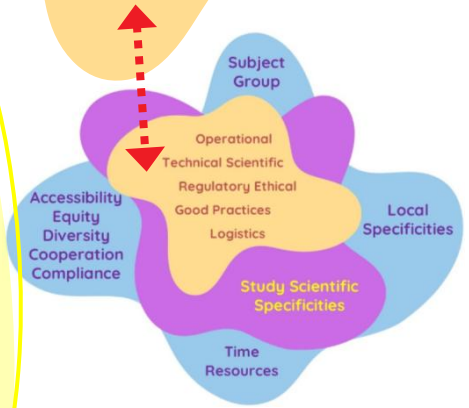

Barr J, Paulson SS, Kamdar B, Ervin JN, Lane-Fall M, Liu V, Kleinpell R. The Coming of Age of Implementation Science and Research in Critical Care Medicine. Crit Care Med. 2021 Aug 1;49(8):1254-1275.Doi: 10.1097/CCM.0000000000005131. PMID: 34261925; PMCID: PMC8549627.

Study Implementation Activities

Implementation Science

- IS includes both implementation research (IR) and practice, with IR forming part of the continuum of translational research → basic science, clinical, and population health-based research, testing novel therapeutic strategies and accelerating these therapeutic interventions into clinical practice with the goal of improving patient outcomes (PRECISION MEDICINE).

- IS is broader than implementation itself; implementation practice uses systematic methods to adopt best practices, whereas IS seeks to understand how/why the adoption of best practices either occurs or fails.

PROJECT

Definitions

Operational

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Regulatory Ethical

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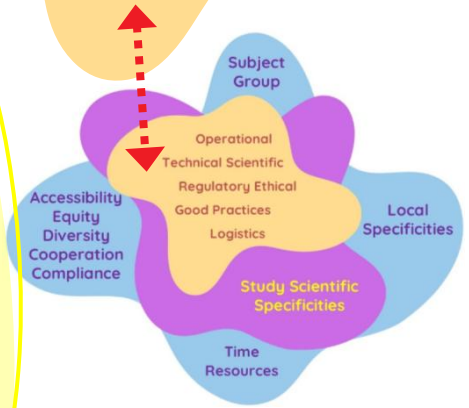
Logistics



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Study Implementation Activities

Implementation Science

- Branch of health services research that uses principles from organizational psychology, public health, operations management, epidemiology, and behavioral economics to evaluate implementation failures and to use this knowledge to develop and test strategies to overcome barriers and to close the evidence practice gap.

- Aims to strengthen the implementation of best practices and the de-implementation of ineffective practices and to ensure the uptake and sustainability of new and existing knowledge and experience. Implementation practice tends to use extant knowledge and tools to address implementation challenges, while IR is often focused on advancing the field of IS itself through the development of theory, measures, and innovative study designs.

PROJECT

INVpath

Definitions

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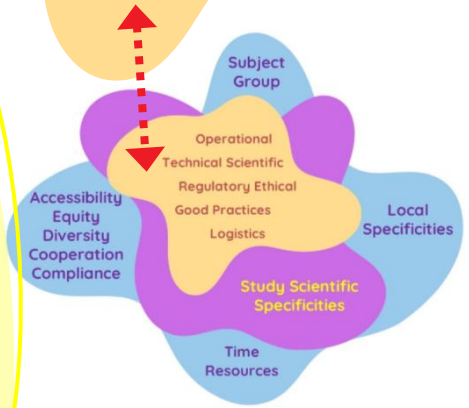
Good Practices

Logistics



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Study Implementation Activities

Implementation Science

- Implementation and effectiveness simultaneously in an approach known as the “effectiveness-implementation hybrid design”, where relationships between implementation and effectiveness can be tested, and intervention effectiveness can be interrogated in clinical settings.
- Implementation is aligned with existing quality initiatives; to characterize implementation determinants and evaluate implementation efforts.
- Flexibility; importance of the context → lessons learned from a local QI effort may or may not translate to other critical care settings. Ideally, IR and implementation practice teams could work together to identify common barriers and facilitators and to identify the most promising implementation strategies.

PROJECT

Definitions

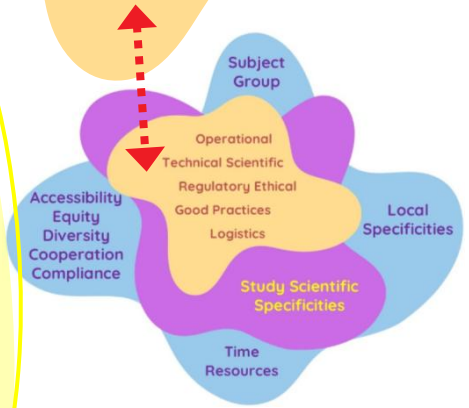
Operational

Technical-Scientific

Regulatory Ethical

Good Practices

Logistics



https://implementationsciencecomms.biomedcentral.com/articles/10.1186/s43058-022-00355-6

Study Implementation Activities

Implementation Science

- Clinical trials can be considered beneficial evidence-based interventions suffering from poor implementation. Adapting implementation science approaches to the clinical trial context can provide frameworks for contextual assessment, outcome measurement, targeted interventions, and a shared vocabulary for clinical trial improvement.

- Additionally, exploring implementation frameworks in the trial context can advance the science of implementation through both “test cases” and providing fertile ground for implementation intervention design and testing.

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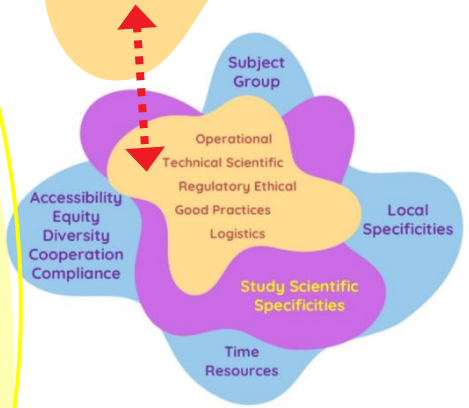

Barr J, Paulson SS, Kamdar B, Ervin JN, Lane-Fall M, Liu V, Kleinpell R. The Coming of Age of Implementation Science and Research in Critical Care Medicine. Crit Care Med. 2021 Aug 1;49(8):1254-1275.Doi: 10.1097/CCM.0000000000005131. PMID: 34261925; PMCID: PMC8549627.

Study Implementation Activities

Implementation Science

"is the interaction between the innovation, the intended adopter(s), and the context that determines the innovation adoption rate"

Identified five major domains of variables that interact to influence the adoption of an innovation:

1) **the characteristics of the innovation (i.e., strength of evidence, relative advantage, compatibility, etc.);**
2) **the inner setting (i.e., the structural and cultural characteristics of the organization);**
3) **the outer setting (i.e., regulatory policies and payment models);**
4) **the characteristics of the individuals involved (i.e., knowledge, beliefs, receptiveness to change); and**
5) **the implementation processes used (e.g., bottom-up vs top-down decision making)**

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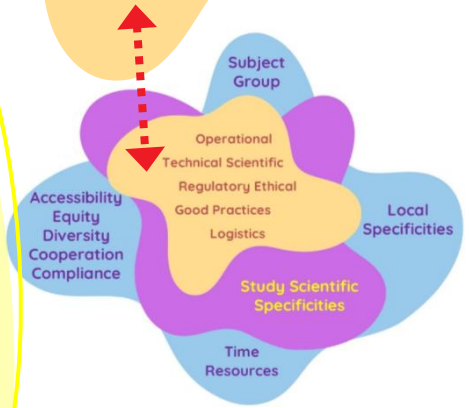

Study Implementation Activities

Study Specific **Operational and Logistical Actions**

driven by the following requirements:

- **Technical-Scientific**
- **Regulatory-Ethical**
- **Guidelines-Good Practices**

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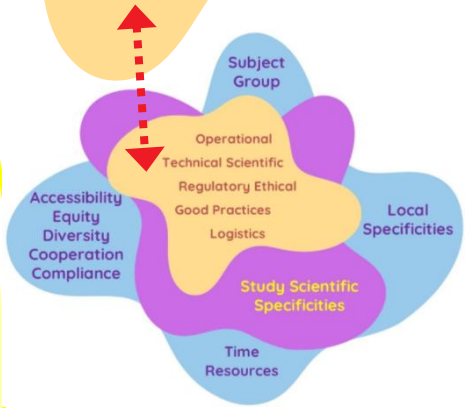

Study Implementation Activities

Technical-Scientific	Study Protocol and Plans
Regulatory-Ethical	Global, Country, Site Regulatory (legal) and Ethical Requirements for Research
Guidelines-Good Practices	ICH Guidelines

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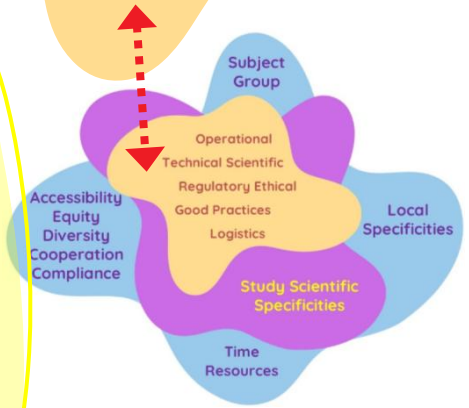

https://processmap.tghn.org/?mapnode=characterise-study-identify-regulations

Study Implementation Activities

Technical-Scientific

Study Protocol and Plans

- What type of study and research is going to be conduct.
- Definition and characterization of the research will guide many of the operational steps and also what regulations and guidelines/plans are required to create and follow.
- The risk and complexity of the protocol, will define many of the requirements in terms of operational needs and also complying with regulatory requirements.

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Study Implementation Activities

Technical-Scientific

Study Protocol and Plans

World Health Organization

SEVENTY-FIFTH WORLD HEALTH ASSEMBLY
Agenda item 16.2

WHA75.8
27 May 2022

Strengthening clinical trials[1] to provide high-quality evidence on health interventions and to improve research quality and coordination

Global action plan for clinical trial ecosystem strengthening

21 April 2025 | Technical document

Overview

This plan sets out nine key action areas to improve innovation, design, conduct, and oversight of clinical trials. It supports implementation of WHO's guidance for best practices for clinical trials and World Health Assembly resolution WHA75.8, aiming to build sustainable, efficient, and inclusive clinical trial ecosystems that generate high-quality evidence to inform policy and practice.

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World Health Organization

SEVENTY-FIFTH WORLD HEALTH ASSEMBLY
Agenda item 16.2

WHA75.8
27 May 2022

Strengthening clinical trials[1] to provide high-quality evidence on health interventions and to improve research quality and coordination

Recognizing that well-designed[1] and well-implemented clinical trials are indispensable for assessing the safety and efficacy of health interventions;

Noting the role of clinical trials in the development of safe and efficacious new health interventions, and in informing associated comparative cost–effectiveness evaluations vis-à-vis existing interventions with a view to promoting the affordability of health products;

Noting also that clinical trials on new health interventions are likely to produce the clearest result when carried out in diverse settings, including all major population groups the intervention is intended to benefit, with a particular focus on under-represented populations;

Recognizing the potential benefits available from collaboration, coordination and the exchange of information between public and non-public funders of clinical trials, while actively preventing and managing conflicts of interest, and noting the potential benefits from public and non-public funders of clinical trials taking steps to ensure funding is targeted towards well-designed and well-implemented clinical trials that will produce actionable evidence regarding health interventions that address public health priorities and in particular the health needs of developing countries, such as neglected tropical diseases, while seeking to strengthen the capability in developing countries to conduct scientifically and ethically sound clinical trials;

Recognizing also the essential contribution of clinical trial participants;

Underscoring that clinical trials should be health-needs driven, evidence based, well designed and well implemented and be guided by established ethical guidance, including principles of fairness, equity, justice, beneficence and autonomy; and that clinical trials should be considered a shared responsibility;

Acknowledging the importance of promoting equity in clinical trial capability, including by enhancing the core competencies of research personnel, ensuring human subject protections from the risks of clinical trials and acknowledging the shared benefits from the results generated from clinical research and development, including clinical trials, both by strengthening the clinical trial global ecosystem to evaluate health interventions and by working to strengthen country capacities to conduct clinical trials that provide the highest protections to human subjects and meet relevant regulations and internationally harmonized standards by considering: (a) systematic assessment of country-level clinical trial capabilities to promote the ability to conduct rigorous clinical trials compliant with international guidelines and the ability to safeguard human subjects; (b) strengthened global clinical trial capabilities, in coordination with existing organizations and structures, in order to promote well-designed and well-implemented clinical trials that produce high-quality evidence, as well as to ensure trials are designed to reflect the heterogeneity of those who will ultimately use or benefit from the intervention being evaluated, and are conducted in diverse settings, including all major population groups the intervention is intended to benefit, with a particular focus on under-represented populations; (c) where possible, inclusion of all trial stakeholders, including representatives of patient groups, according to best practices in the development of clinical trials with affected communities to ensure that the health interventions address their needs, such as solutions on neglected tropical diseases; (d) that clinical trial participants include all major population groups that the intervention is intended to benefit;

Study Implementation Activities

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Study Protocol and Plans

“Underscoring that clinical trials should be health-needs driven, evidence based, well designed and well implemented and be guided by established ethical guidance, including principles of fairness, equity, justice, beneficence and autonomy; and that clinical trials should be considered a shared responsibility“

“Set the stage for ongoing dialogue and collaboration among global clinical trial stakeholders. The expected outcome is a comprehensive action plan that will guide efforts to bolster clinical research capabilities worldwide, ensuring better health outcomes for all.”

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Study Implementation Activities

Open Source
Tools & Platforms

Technical-Scientific

Study Protocol and Plans

Identification of *Open Source* Platforms for:

Valid sources for information and tools to develop health research activities:

- **Guidelines; Instructions; Recommendations;**
- **Templates of essential documents, study protocol, procedures and plans;**
- **Training materials;**
- **Data analysis and software.**

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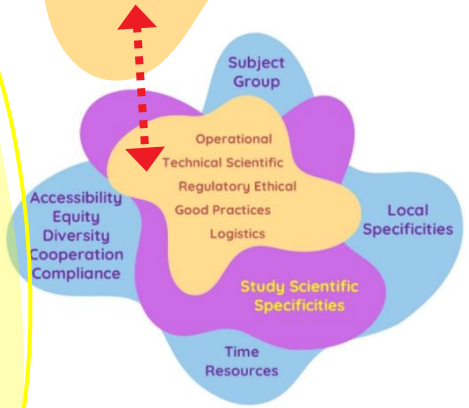

https://www.thelancet.com/journals/langlo/article/PIIS2214-109X%2824%2900515-1/fulltext

Study Implementation Activities

Regulatory-Ethical

Global, Country, Site Regulatory (legal) and Ethical Requirements for Research

- Regulatory authorities as well as research ethics committees and institutional review boards (RECs and IRBs) are the independent entities responsible for approving clinical trials initiation and providing oversight, irrespective of the substantial variation in roles and responsibilities of these bodies across countries and jurisdictions
- Robust regulatory and ethics review systems safeguards and oversight research → ensuring that research is conducted ethically, with rigorous scientific standards, proper safety and high-quality.

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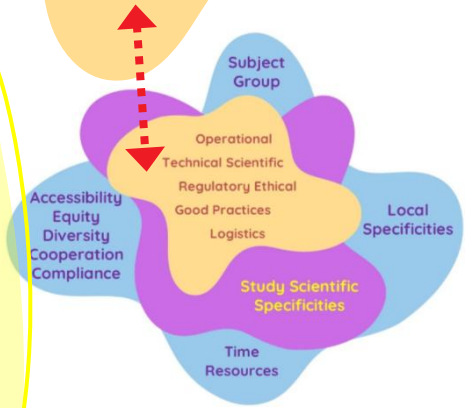

Study Implementation Activities

Regulatory-Ethical

Global, Country, Site Regulatory (legal) and Ethical Requirements for Research

Both the ICH GCP E6(R3)[2] and the Declaration of Helsinki stress that no study should be initiated without ethical review[2-4] of its design, procedures and key documents, including the protocol, informed consent, and investigator's brochure. Review by an IRB/IEC ensures that the rights, safety, well-being, and risk-benefit balance is favourable and ethical for each participant, especially for those in vulnerable conditions.

Important: Ethics Committee approval is not only a regulatory requirement, but also a critical component for the scientific and ethical validity of the study[2-5].

ICH Good Clinical Practice E6(R3) • Global Health Training Centre

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Research need to be approved by committees required by:

1. Country's legal requirements
2. Institutional requirements
3. Funder's requirements
4. Collaborator requirements

Study Implementation Activities

Regulatory-Ethical

Global, Country, Site Regulatory (legal) and Ethical Requirements for Research

Ethics Committees **comprise a nr. of members, who collectively have the qualifications and experience to review and evaluate the science, medical aspects, and ethics of the proposed trial. ICH GCP recommends to include at least 5 members; at least 1 member whose primary area of interest is non-scientific; at least 1 member who is independent of the institution/site. Only those EC members who are independent of the investigator and the sponsor of the trial should vote/provide opinion on a trial-related matter.**

https://processmap.tghn.org/?mapnode=submit-ethics-review

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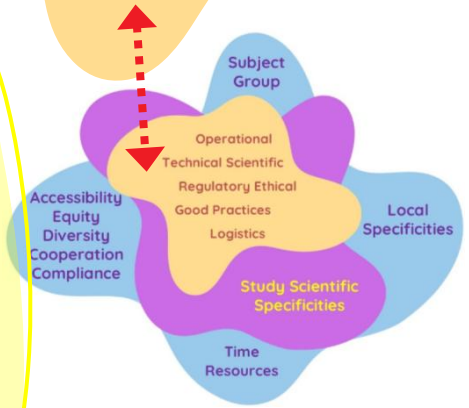

https://processmap.tghn.org/?mapnode=clinical-trial-authority-review

Study Implementation Activities

Regulatory-Ethical

Global, Country, Site Regulatory (legal) and Ethical Requirements for Research

A **Regulatory Agency** is an organization that oversees clinical research within a specific area or jurisdiction. In contrast, a **National Regulatory Authority** (NRA) oversees the full spectrum of regulatory processes related to product development, such as clinical trial approval and market authorization at the national level.

It's important to check the authorities involved for each country in your research and procedure requirements. NRAs are responsible for ensuring that clinical trials are scientifically sound, that they will result in data that will support regulatory decision making, and that the rights and safety of clinical trial participants are protected.

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Regulatory-Ethical

Global, Country/Local Regulatory (legal) and Ethical Requirements for Research

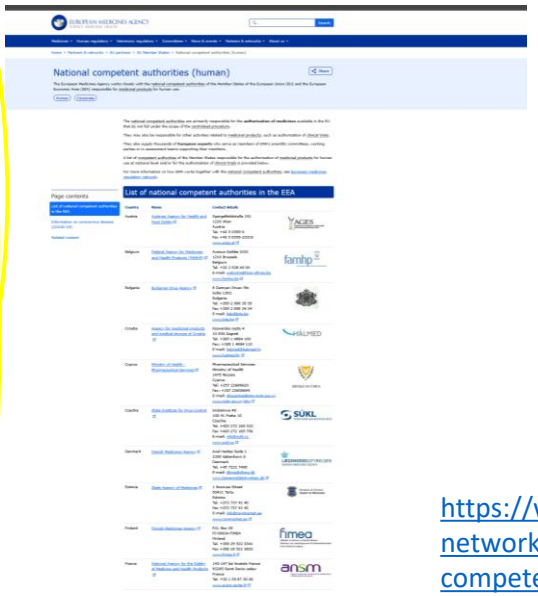
https://clinregs.niaid.nih.gov/

International Regulatory Agencies

e.g. FDA, EMA, AMA

National Competent Authorities

e.g. INFARMED, AEMPS, MHCTR



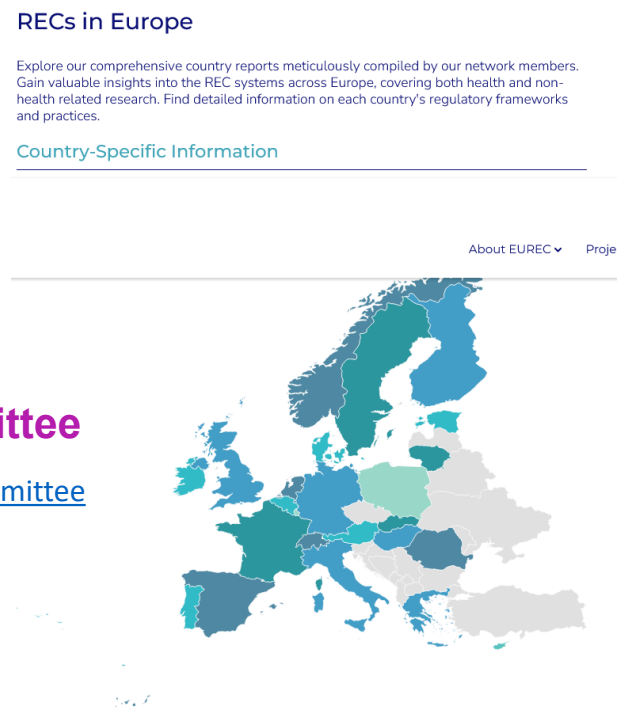
https://www.ema.europa.eu/en/partners-networks/eu-partners/eu-member-states/national-competent-authorities-human

WHO Research Ethics Review Committee

https://www.who.int/groups/research-ethics-review-committee

EU National Research Ethics Committees

https://eurecnet.eu/about-eurec/about-us/



Austria | Belgium | Cyprus | Denmark | Estonia | Finland | Germany | Greece | Hungary | Ireland | Italy | Lithuania | Luxembourg | Netherlands | Norway | Poland | Portugal | Romania | Slovakia | Spain | Sweden | Switzerland | France | United Kingdom

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https://www.ich.org/

International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH)

ICH Guidelines

The ICH topics are divided into the four categories below and ICH topic codes are assigned according to these categories.

Quality Guidelines

Harmonisation achievements in the Quality area include pivotal milestones such as the conduct of stability studies, defining relevant thresholds for impurities testing and a more flexible approach to pharmaceutical quality based on Good Manufacturing Practice (GMP) risk management.

Safety Guidelines

ICH has produced a comprehensive set of safety Guidelines to uncover potential risks like carcinogenicity, genotoxicity and reprotoxicity. A recent breakthrough has been a non-clinical testing strategy for assessing the QT interval prolongation liability: the single most important cause of drug withdrawals in recent years.

Efficacy Guidelines

The work carried out by ICH under the Efficacy heading is concerned with the design, conduct, safety and reporting of clinical trials. It also covers novel types of medicines derived from biotechnological processes and the use of pharmacogenetics/genomics techniques to produce better targeted medicines.

Multidisciplinary Guidelines

Those are the cross-cutting topics which do not fit uniquely into one of the Quality, Safety and Efficacy categories. It includes the ICH medical terminology (MedDRA), the Common Technical Document (CTD) and the development of Electronic Standards for the Transfer of Regulatory Information (ESTRI).

Home \ ICH Guidelines \ Efficacy Guidelines

Efficacy Guidelines

The work carried out by ICH under the Efficacy heading is concerned with the design, conduct, safety and reporting of clinical trials. It also covers novel types of medicines derived from biotechnological processes and the use of pharmacogenetics/ pharmacogenomics techniques to produce better targeted medicines.

- E1 Clinical Safety for Drugs used in Long-Term Treatment
- E2A - E2F Pharmacovigilance
- E3 Clinical Study Reports
- E4 Dose-Response Studies
- E5 Ethnic Factors
- E6 Good Clinical Practice
  - E6(R2) Good Clinical Practice (GCP)
  - E6(R3) EWG Good Clinical Practice (GCP)
  - E6(R3) Good Clinical Practice (GCP) Annex-2 Sub-Group

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ICH Guidelines

International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH)

Good Clinical Practice (GCP)

Standard for the planning, initiating, performing, recording, oversight, evaluation, analysis and reporting of clinical trials that provides assurance that the data and reported results are reliable and that the rights, safety and well-being of trial participants are protected.

https://database.ich.org/sites/default/files/ICH_E6%28R3%29_Step4_FinalGuideline_2025_0106.pdf

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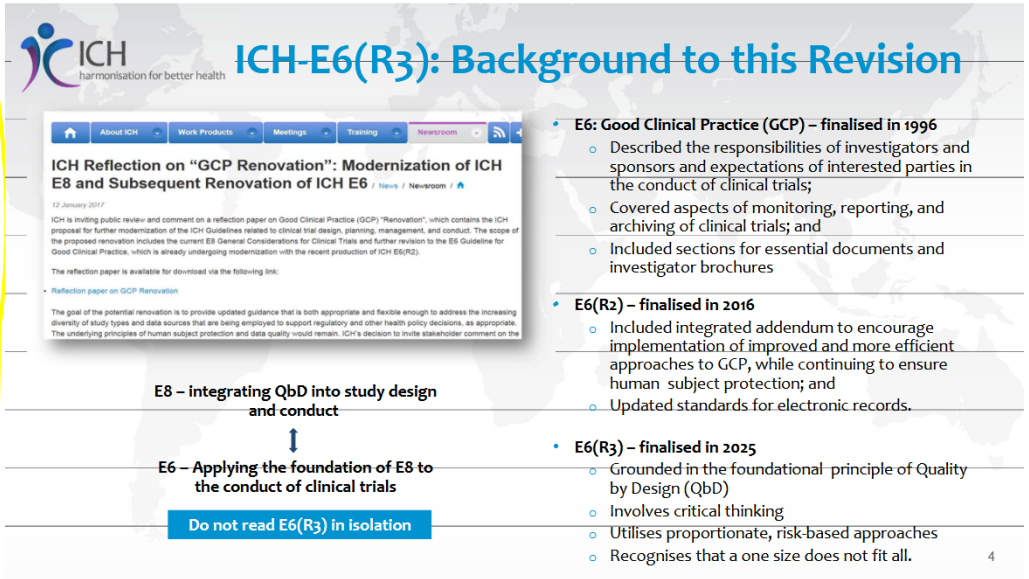

ICH harmonisation for better health

ICH-E6(R3): Background to this Revision

ICH Reflection on "GCP Renovation": Modernization of ICH E8 and Subsequent Renovation of ICH E6 / News / Newsroom /

12 January 2017

ICH is inviting public review and comment on a reflection paper on Good Clinical Practice (GCP) "Renovation", which contains the ICH proposal for further modernization of the ICH Guidelines related to clinical trial design, planning, management, and conduct. The scope of the proposed renovation includes the current E8 General Considerations for Clinical Trials and further revision to the E6 Guideline for Good Clinical Practice, which is already undergoing modernization with the recent production of ICH E6(R2).

The reflection paper is available for download via the following link:

- Reflection paper on GCP Renovation

The goal of the potential renovation is to provide updated guidance that is both appropriate and flexible enough to address the increasing diversity of study types and data sources that are being employed to support regulatory and other health policy decisions, as appropriate. The underlying principles of human subject protection and data quality would remain. ICH's decision to invite stakeholder comment on the

E8 – integrating QbD into study design and conduct

↕

E6 – Applying the foundation of E8 to the conduct of clinical trials

Do not read E6(R3) in isolation

- **E6: Good Clinical Practice (GCP) – finalised in 1996**
  - Described the responsibilities of investigators and sponsors and expectations of interested parties in the conduct of clinical trials;
  - Covered aspects of monitoring, reporting, and archiving of clinical trials; and
  - Included sections for essential documents and investigator brochures
- **E6(R2) – finalised in 2016**
  - Included integrated addendum to encourage implementation of improved and more efficient approaches to GCP, while continuing to ensure human subject protection; and
  - Updated standards for electronic records.
- **E6(R3) – finalised in 2025**
  - Grounded in the foundational principle of Quality by Design (QbD)
  - Involves critical thinking
  - Utilises proportionate, risk-based approaches
  - Recognises that a one size does not fit all.

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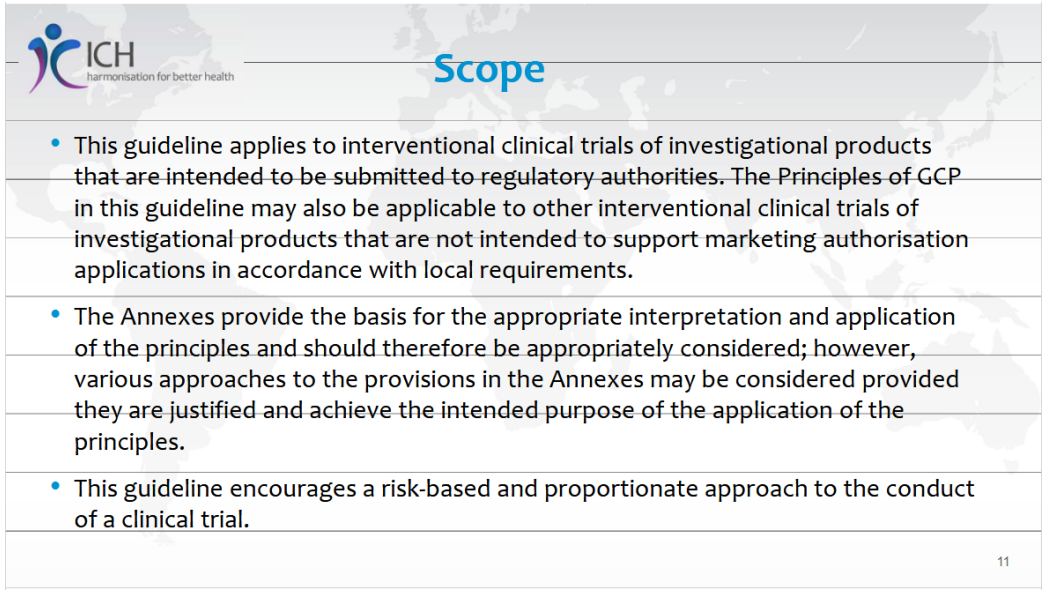

ICH harmonisation for better health

Scope

- This guideline applies to interventional clinical trials of investigational products that are intended to be submitted to regulatory authorities. The Principles of GCP in this guideline may also be applicable to other interventional clinical trials of investigational products that are not intended to support marketing authorisation applications in accordance with local requirements.
- The Annexes provide the basis for the appropriate interpretation and application of the principles and should therefore be appropriately considered; however, various approaches to the provisions in the Annexes may be considered provided they are justified and achieve the intended purpose of the application of the principles.
- This guideline encourages a risk-based and proportionate approach to the conduct of a clinical trial.

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https://database.ich.org/sites/default/files/ICH_E6%28R3%29_Step%204_Presentation_2025_0123.pdf

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Revised Structure

E6(R3) Guideline

- I. INTRODUCTION
- II. PRINCIPLES OF ICH GCP
- III. ANNEX 1
  1. Institutional Review Board/Independent Ethics Committee (IRB/IEC)
  2. Investigator
  3. Sponsor
  4. Data Governance – Investigator and Sponsor

E6(R3) Principles and Annex 1 replacing E6(R2)

- APPENDICES
  - Appendix A. Investigator's Brochure
  - Appendix B. Clinical Trial Protocol and Protocol Amendment(s)
  - Appendix C. Essential Records for the Conduct of a Clinical Trial
- GLOSSARY

ANNEX 2 – *under public consultation from November 2024 to March 2025*

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ICH E6(R3) Principle

ICH E6(R3) PRINCIPLE	TOPIC	ICH E6(R2) PRINCIPLE
1	Ethical Principles	2.1, 2.2, 2.3, 2.7, 2.11
2	Informed Consent	2.9
3	IRB/IEC Review	2.6
4	Science	2.4, 2.5
5	Qualified Individuals	2.8
6	Quality	2.13
7	Risk Proportionality	N/A
8	Protocol	2.5
9	Reliable Results	2.10
10	Roles and Responsibilities	N/A
11	Investigational Products	2.12

https://database.ich.org/sites/default/files/ICH_E6%28R3%29_Step%204_Presentation_2025_0123.pdf

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Innovation, Efficiency & Engagement

- Encouraging the exploration of technology:
  - The principles are intended to support efficient approaches to trial design and conduct. For example, innovative digital health technologies, such as wearables and sensors may expand the possible approaches to trial conduct.
  - Such technologies can be incorporated into existing healthcare infrastructures and enable the use of a variety of relevant data sources in clinical trials.
  - The use of technology in the conduct of clinical trials should be adapted to fit the participant characteristics and the particular trial design.
- Encouraging engagement and inclusivity:
  - The use of innovative trial designs and technologies may enable the inclusion of a wider and more diverse population of participants and thereby broaden the applicability of trial outcomes.
  - The design and conduct of the clinical trial may be supported by obtaining the perspectives of interested parties, such as patients and their communities, patient advocacy groups and healthcare professionals. Their input can help to reduce unnecessary complexity, improve feasibility and increase the likelihood of meaningful trial outcomes.

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3.10.1 Risk Management

A proportionate approach to the identification and management of risk is described below:

3.10.1.1 Risk Identification

The sponsor should identify risks that may have a meaningful impact on critical to quality factors prior to trial initiation and throughout trial conduct. Risks should be considered across the processes and systems, including computerised systems, used in the clinical trial (e.g., trial design, participant selection, informed consent process, randomisation, blinding, investigational product administration, data handling and service provider activities).

3.10.1.2 Risk Evaluation

The sponsor should evaluate identified risks and existing controls in place to mitigate the risk by considering:

(a) The likelihood of harm/hazard occurring;

(b) The extent to which such harm/hazard would be detectable;

(c) The impact of such harm/hazard on trial participant protection and the reliability of trial results.

3.10.1.3 Risk Control

Risk control should be proportionate to the importance of the risk to participants' rights, safety and well-being and the reliability of trial results. Risk mitigation activities may be incorporated, for example, in protocol design and implementation, monitoring plans, agreements between parties defining roles and responsibilities, and training.

Where relevant, the sponsor should set pre-specified acceptable ranges (e.g., quality tolerance limits at the trial level) to support the control of risks to critical to quality factors. These pre-specified ranges reflect limits that when exceeded have the potential to impact participant safety or the reliability of trial results. Where deviation beyond these ranges is detected, an evaluation should be performed to determine if there is a possible systemic issue and if action is needed.

3.10.1.4 Risk Communication

The sponsor should document and communicate the identified risks and mitigating activities, if applicable, to those who are involved in taking action or are affected by such activities. Communication also facilitates risk review and continual improvement during clinical trial conduct.

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3.10 Quality Management

The sponsor should implement an appropriate system to manage quality throughout all stages of the trial process. Quality management includes the design and implementation of efficient clinical trial protocols, including tools and procedures for trial conduct (including for data collection and management), in order to ensure the protection of participants' rights, safety and well-being and the reliability of trial results. The sponsor should adopt a proportionate and risk-based approach to quality management, which involves incorporating quality into the design of the clinical trial (i.e., quality by design) and identifying those factors that are likely to have a meaningful impact on participants' rights, safety and well-being and the reliability of the results (i.e., critical to quality factors as described in ICH E8(R1)). The sponsor should describe the quality management approach implemented in the trial in the clinical trial report (see ICH E3 Structure and Content of Clinical Study Reports).

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3.11.4.1 Investigator Site Monitoring

(a) Monitoring may be performed in relation to the clinical trial activities at the investigator sites (including their pharmacies and local laboratories, as appropriate). The frequency of monitoring activities should also be determined based on identified risks. Monitoring activities and their frequency should be modified as appropriate using knowledge gained.

(b) This monitoring activity may be performed on-site and/or remotely depending on the nature of the activity and its objectives.

(c) Monitoring may include remote and secure, direct read-only access to source records, other data acquisition tools and essential record retention systems.

3.11.4.2 Centralised Monitoring

(a) Centralised monitoring is an evaluation of accumulated data, performed in a timely manner, by the sponsor's qualified and trained persons (e.g., medical monitor, data scientist/data manager, biostatistician).

(b) Centralised monitoring processes provide additional monitoring capabilities that can complement and reduce the extent and/or frequency of site monitoring or be used on its own. Use of centralised data analytics can help identify systemic or site-specific issues, including protocol noncompliance and potentially unreliable data.

(c) Centralised monitoring may support the selection of sites and/or processes for targeted site monitoring.

3.11.4 Monitoring

The aim of monitoring is to ensure the participants' rights, safety and well-being and the reliability of trial results as the trial progresses. Monitoring is one of the principal quality control activities.

Monitoring involves a broad range of activities including, but not limited to, communication with investigator sites, verification of the investigator and investigator site staff qualifications and site resources, training and review of trial documents and information using a range of approaches including source data review, source data verification, data analytics and visits to institutional facilities undertaking trial-related activities. Some of these monitoring activities (e.g., centralised monitoring) may be conducted by different methods and persons with different roles (e.g., data scientist). However, monitoring should be performed by persons not involved in the clinical conduct of the trial at the site being monitored. The monitoring approach should consider the activities and services involved, including decentralised settings, and be included in the monitoring plan. Monitors and other trial staff should adhere to data protection and confidentiality requirements in accordance with applicable regulatory requirements, institution policy and established data security standards.

https://database.ich.org/sites/default/files/ICH_E6%28R3%29_Step4_FinalGuideline_2025_0106.pdf

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INVpath

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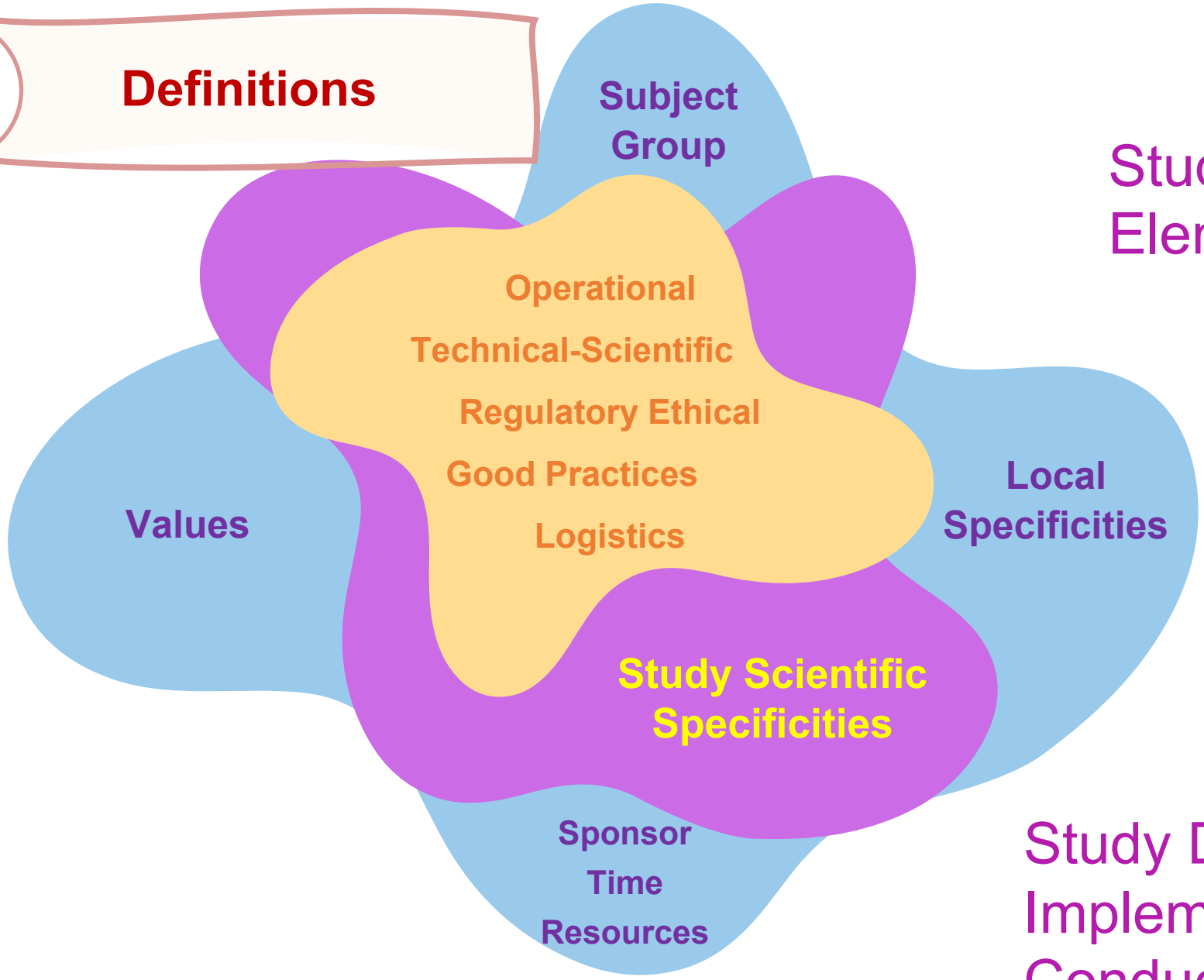


Study Essential Elements Matrix

Study Development, Implementation and Conduct Activities

PROJECT

Definitions

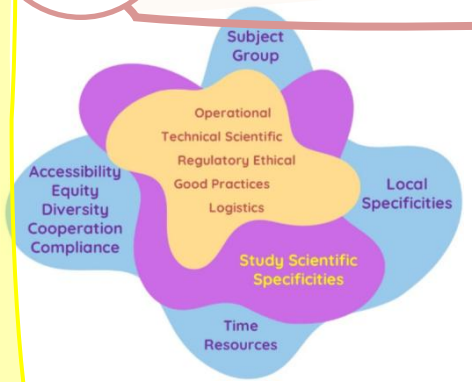
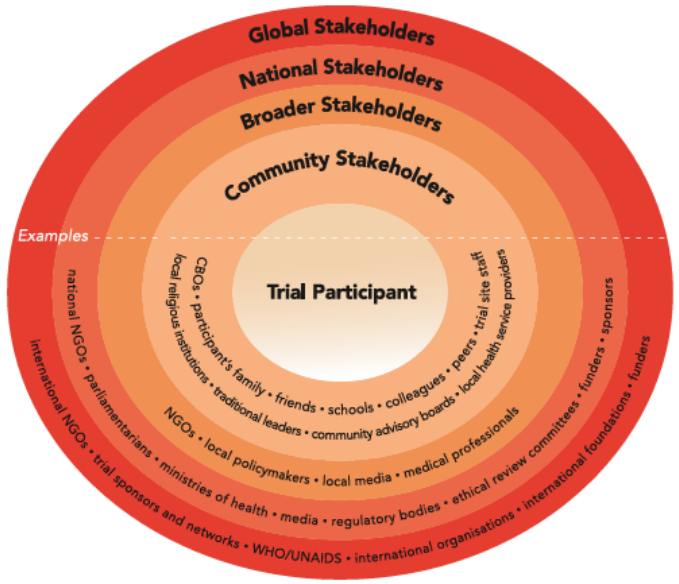
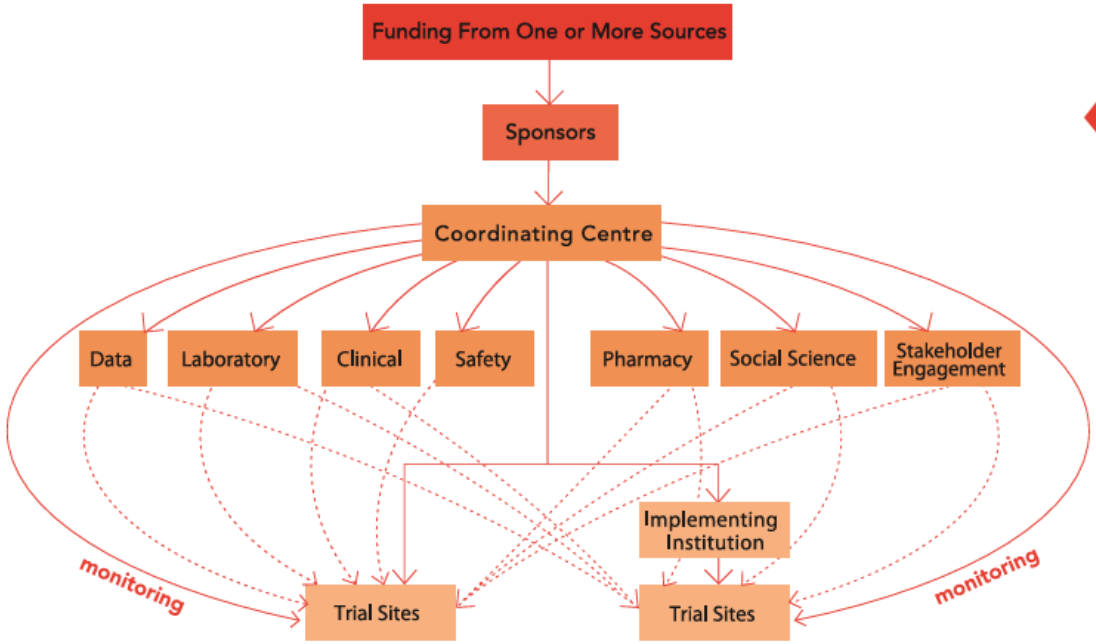


Figure 2. Layers of Biomedical HIV Prevention Trial Stakeholders



Various stakeholders may influence or be affected by a biomedical HIV prevention trial. Stakeholders include trial participants and other community stakeholders as well as a broader range of national and international stakeholders.

Figure 3. Example of a Trial Network

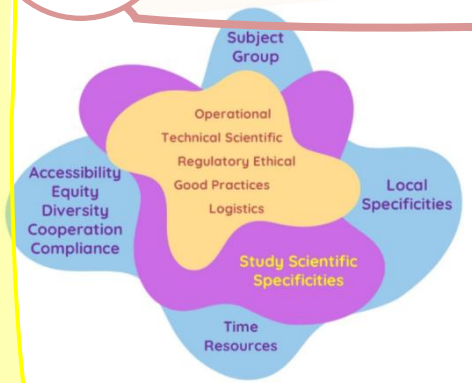


Basic structure of a typical biomedical HIV prevention trial network. Funding from one or more sources is distributed through a network coordinating centre directly to trial sites or to implementing institutions such as universities that then send funds to trial sites. Trial networks may have several centres responsible for different aspects of trial conduct: data management, laboratory, pharmacy, clinical, safety, social science, and stakeholder engagement. Monitoring of trial conduct may be executed through the coordinating centre or outsourced to an independent monitoring organisation.

[Good Participatory Practice: Guidelines for biomedical HIV prevention trials, second edition - AVAC]

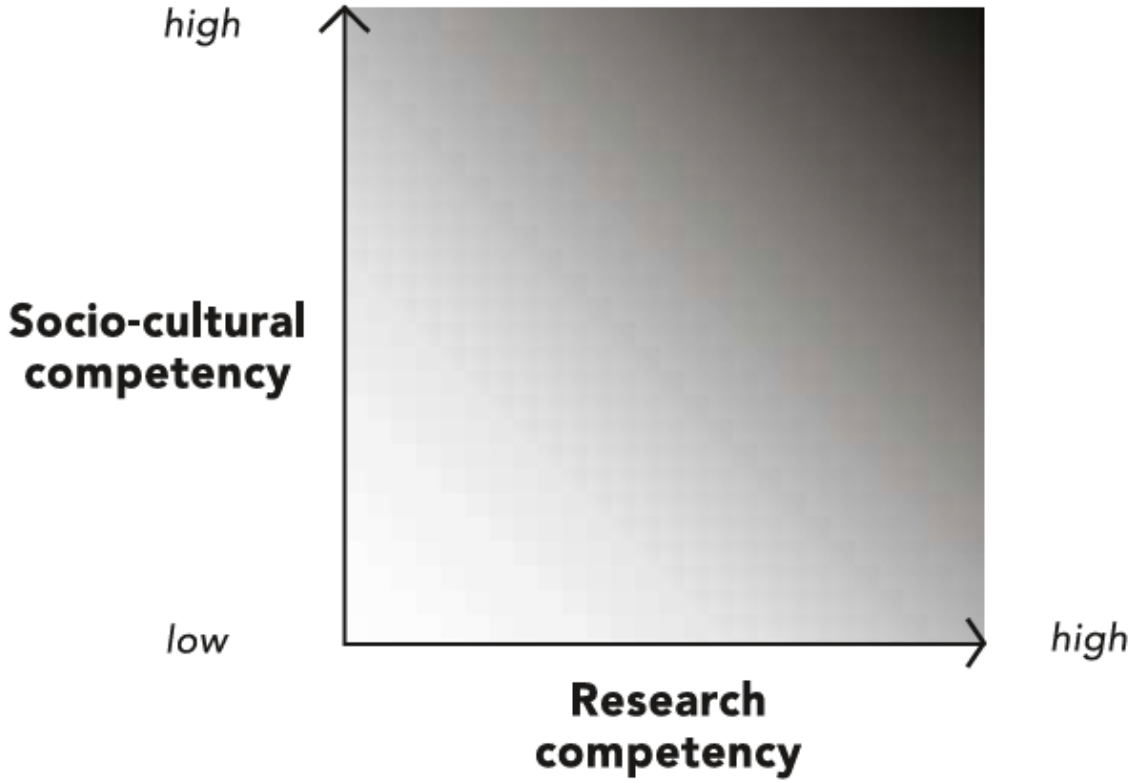
PROJECT

Definitions



[Good Participatory Practice: Guidelines for biomedical HIV prevention trials, second edition - AVAC]

Figure 4. Trial Competency Range



Socio-cultural and research competency are shown as gradients along two axes. Individual stakeholders start their involvement at a particular position on the graph, based on their socio-cultural competency and their research competency. A principal investigator new to a particular location may have high research competency but low socio-cultural competency at the start of the design phase of a trial. A community stakeholder new to biomedical HIV prevention research may have high socio-cultural competency but low research competency when their involvement with a trial begins. All stakeholders share ongoing responsibility to review and strengthen both socio-cultural and research competencies in order to improve mutual understanding.

PROJECT

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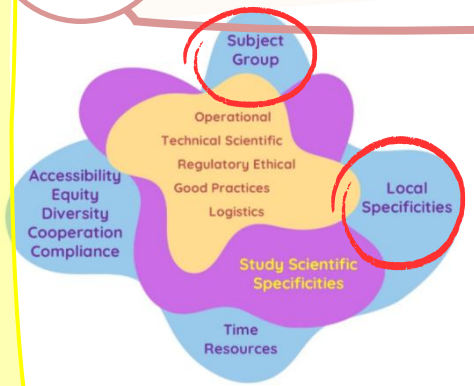
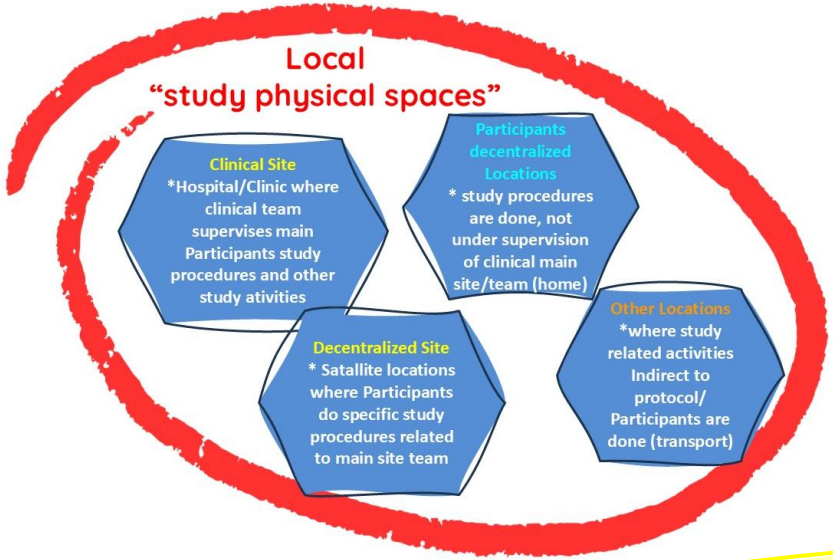
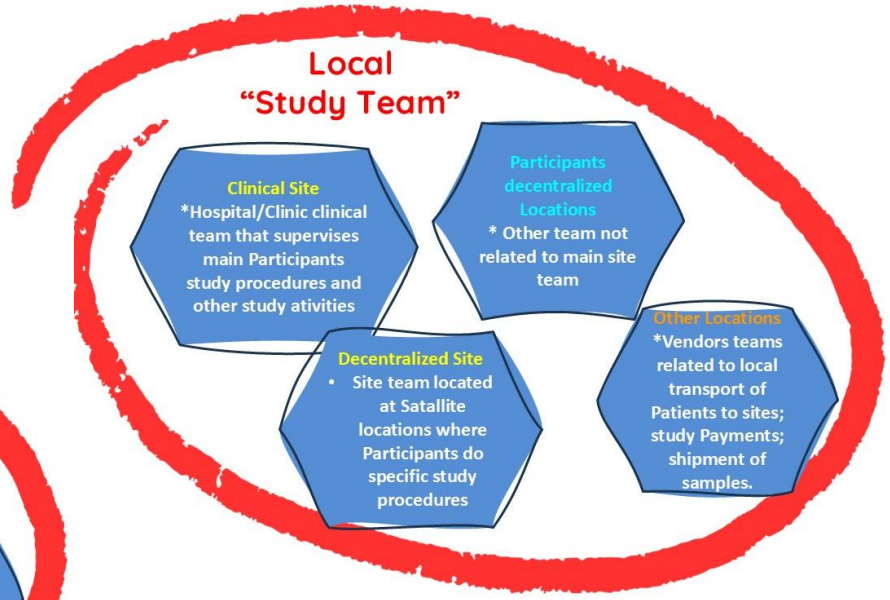
Definitions



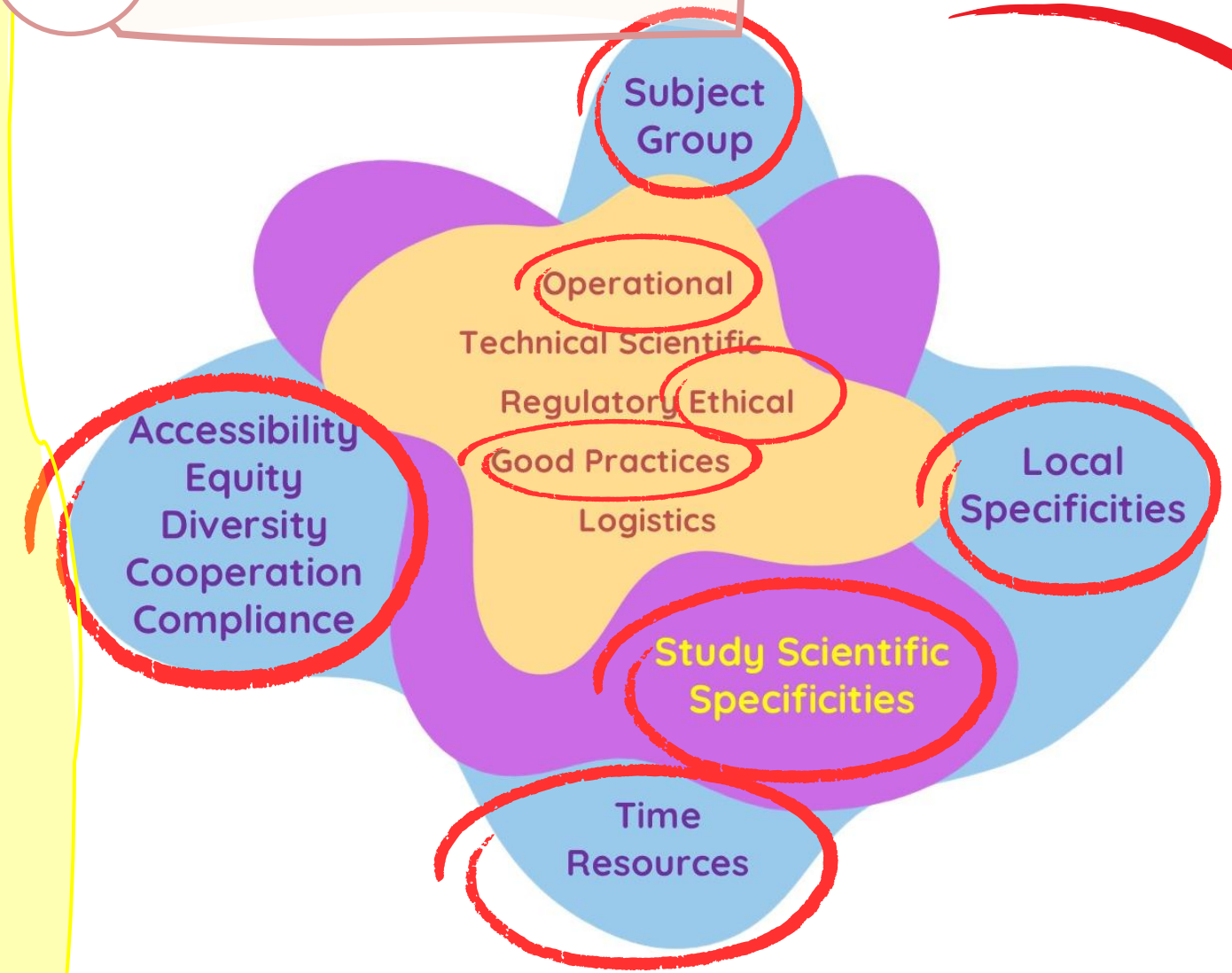




What "spaces" do citizens organizations and community groups (can) occupy in Clinical Research?

PROJECT

Definitions



"Participation spaces"

citizen and community organizations,

enhancing research study development, implementation, conduct and impact.

PROJECT

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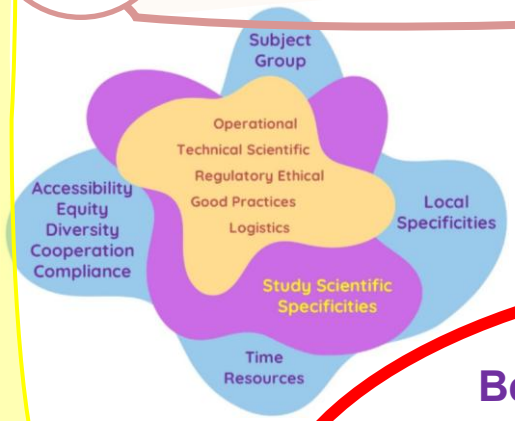
Definitions



What "participation spaces" do community groups can have in the study?

Be "study providers", mainly in decentralized studies, supporting Patient's recruitment, compliance with study procedures, follow up and safety reporting; new "community space located in a neighborhood" where study procedures can be conducted.

Significant Ethical Impact in the Research Ecosystem, enhancing accessibility, equity, safety, compliance, representativity and implementation of studies with real world impact (RWE).

Advisors at different phases of the study: protocol development, study feasibility, qualification, implementation/development.

Promote Local Research and Community Data; be a member of Global Research Consortium financing Independent research aligned with community needs and reality.

PROJECT

Definitions

Intelligent health monitoring: Why community data must be part of the system

21 Jul 2025
ITPC Global

ITPC

About Our Work Our Voices Resources Join The Fight Donate

Our Work

ITPC is an issue-based coalition. We actively advocate for universal treatment access through the following areas of work:

Build Resilient Communities

Watch What Matters

make medicines affordable
END UNFAIR MONOPOLIES

ITPC innovation LAB

ITPC

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About Our Work Our Voices Resources Join The Fig

We are researchers: ITPC Annual Review 2024

Posted on June 2, 2025 by

Annual Reports English

Download

Our 2024 Annual Review, ***We are researchers: using community evidence to drive change***, reflects our commitment to putting community-led research at the heart of global health advocacy. We've seen firsthand how grassroots data and activism can drive real policy change and improve health outcomes. We also mark 10 years of Make Medicines Affordable and continue to push for fairer global health financing through initiatives like the Health ImPACT Coalition.

> Data without people isn't intelligence, it's noise. What real intelligence requires is scale plus speed, but also context.

https://itpcglobal.org/2025/07/21/intelligent-health-monitoring-why-community-data-must-be-part-of-the-system/

PROJECT

Definitions

Enhance Support for Community Leadership

- Commit to providing sustained and adequate funding and resources to community-led organizations to secure their operational capacity and impact.
- Equip national and regional plans with resources to bolster peer-led responses, expand community health education, and enhance recruitment and retention of skilled health workers from underserved populations.
- Ensure key communities play an active role in policy and program design, addressing critical social determinants of health such as housing, employment, and access to education.
- Simplify bureaucratic processes to enable seamless funding access and provide protections for community-led initiatives, particularly in challenging political environments.

Ensure Monitoring with Representation of key community stakeholders

- Ensure diverse community representation in the monitoring of national, regional, and international responses to HIV, TB, and viral hepatitis, embedding their voices at every stage of decision-making processes.
- Facilitate monitoring systems driven by communities, co-developing specific indicators to assess support provided and contributions to health and social outcomes, fostering transparency and accountability.

Implementing these recommendations will empower community-led health responses, ensuring inclusive participation, accountability, and measurable progress toward sustainable and equitable health outcomes.

Responsive and Sustainable Full Spectrum Harm Reduction

Effective harm reduction requires integrated responses that prioritise community leadership[22]. Peers provide invaluable insights into local risk environments, and peer-led programmes have proven to be cost-effective. Collaborations between public health systems and community-led organizations enhance effectiveness, reduce costs, and improve the efficiency of national HIV responses[23].

It is time to scale up community-led responses, ensuring equitable participation, accountability, and measurable impact, committing to leave no one behind and prioritising investment in community-led initiatives.

Vulnerable Populations and underrepresented ACTION

Integration into the Global Health Research Ecosystem

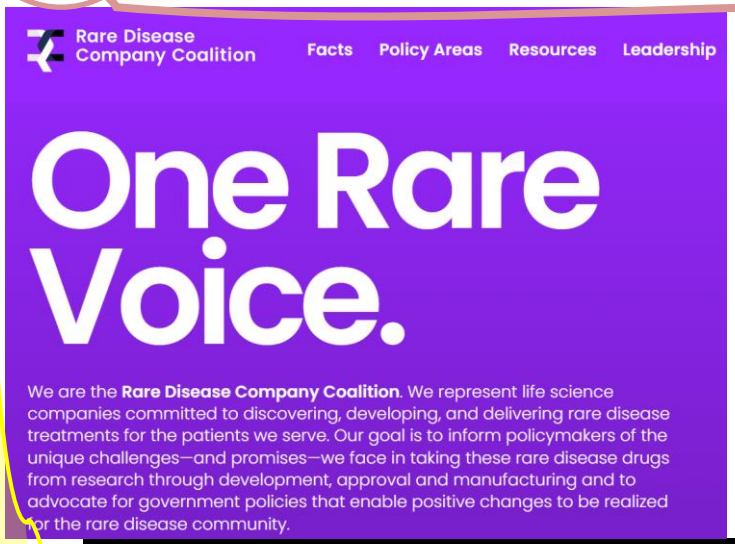
Mitigation of Social Determinants Factors limiting Clinical Research Implementation:

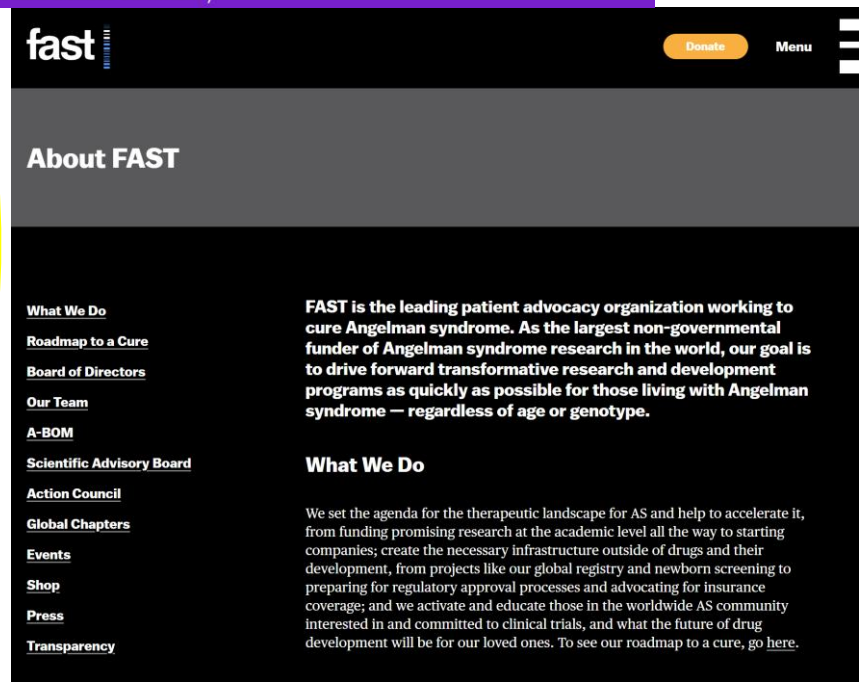
- Advisors on Health Programs;
- Identification of needs that underly Research Purpose;
- Protocol Designs and at all stages of the studies life cycle, including at Ethical Evaluation, Safety and data monitoring systems, study results outcomes sharing among Participant Populations.
- Community organizations and stakeholders with capacity to promote valid and meaningful health research;
- Real World Health Data collected by Community that contributes to overall decisions on Programs and resources distribution within the Research Ecossystem.

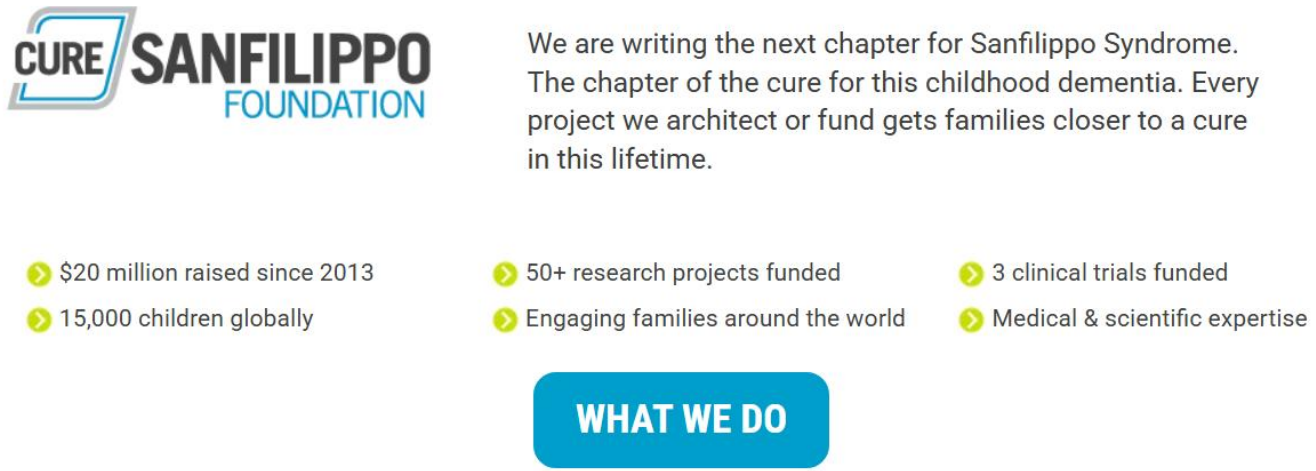
https://www.euronpud.net/wp-content/uploads/2025/07/Scaling-Up-Community-Involvement.pdf

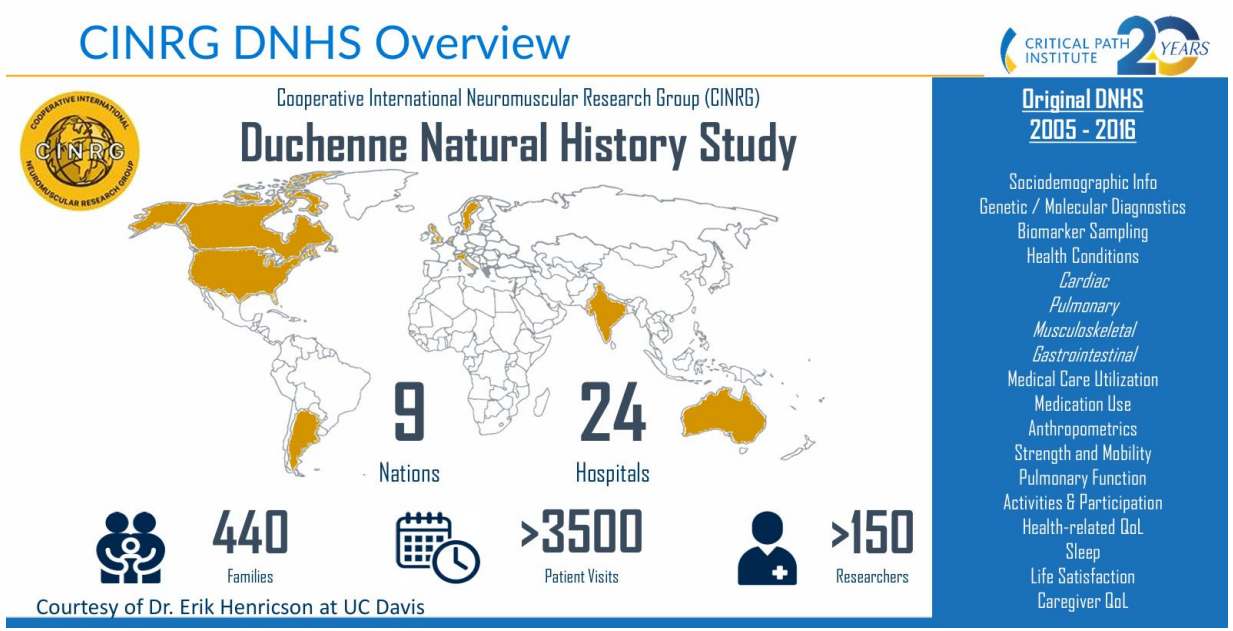
PROJECT

Definitions









[On the RISE: Controls in Rare Disease Clinical Trials for Small and Diminishing Populations]

PROJECT

Definitions

BY NICOLE A COLWELL, MD, AND KIMBERLY DEMIRHAN, MBA, BSN, RN

Bringing Cancer Research to the Community: Strategic Approaches to Representative Oncology Clinical Trial Design

To effectively advance these strategic actions, more formally structured partnerships are needed among the following key stakeholders:

- Government agencies (eg, FDA, NIH, Centers for Medicare & Medicaid Services)
- Oncology professional societies
- Patient advocacy groups
- Industry partners
- Academic institutions
- Community cancer centers
- Health care networks

Several key themes emerged from the discussion that characterized actionable strategies to promote fair and accessible clinical trial design that is representative of all patients with cancer:

- Strengthen the clinical trial workforce.
- Optimize trial design to reflect real-world patient populations.
- Engage with communities outside of clinical trial interactions.
- Expand research access through decentralized clinical trials (DCTs).
- Leverage artificial intelligence (AI) and digital health tools for clinical trial efficiency.

ACCC COMMUNITY ONCOLOGY RESEARCH INSTITUTE

Home / Learn / Community Oncology Research / ACCC Community Oncology Research Institute

ACCC COMMUNITY ONCOLOGY RESEARCH INSTITUTE

Approximately 85% of all patients with cancer are diagnosed and treated in community settings. Despite this, only 3% of those patients are enrolled in clinical trials. Inadequate time, infrastructure, resources, incentives, and reimbursement all contribute to this sparse participation rate.

To address this disparity, the ACCC Community Oncology Research Institute (ACORI) was launched in 2021. ACORI's mission is to establish clinical trials as a standard of care for all patients, regardless of where they are treated, by helping community oncology programs access the tools, knowledge sharing, effective practices, and peer mentorships that can increase their ability to offer clinical trials.

52-62_acori_whitepaper.pdf

ACCC Community Oncology Research Institute

PROJECT

INVpath

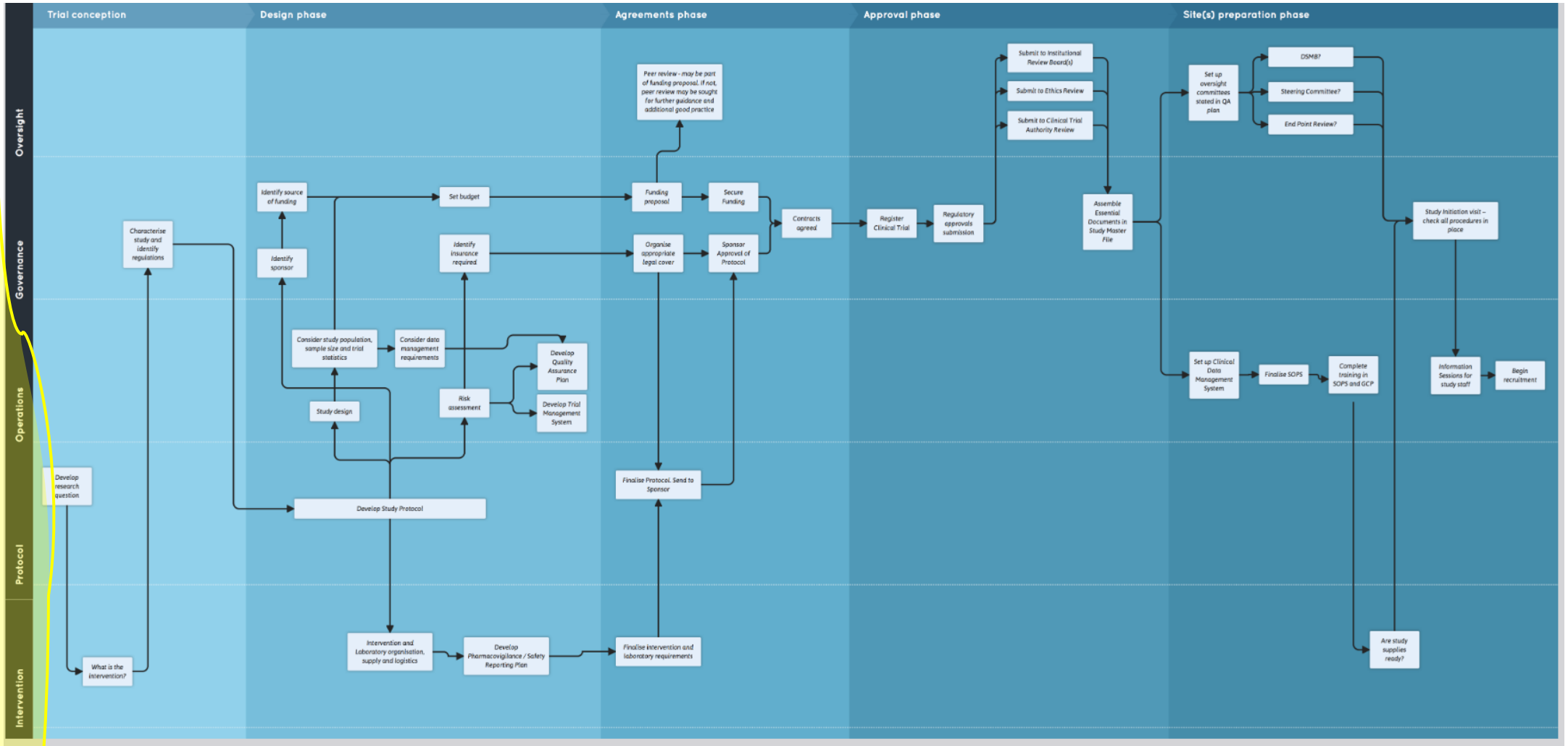
Definitions

Defining each step of a Study Life Cycle

PROJECT

Definitions

Study Life Cycle



https://globalhealthtrials.tghn.org/resources/downloadable-tools-and-templates/

P R O J E C T

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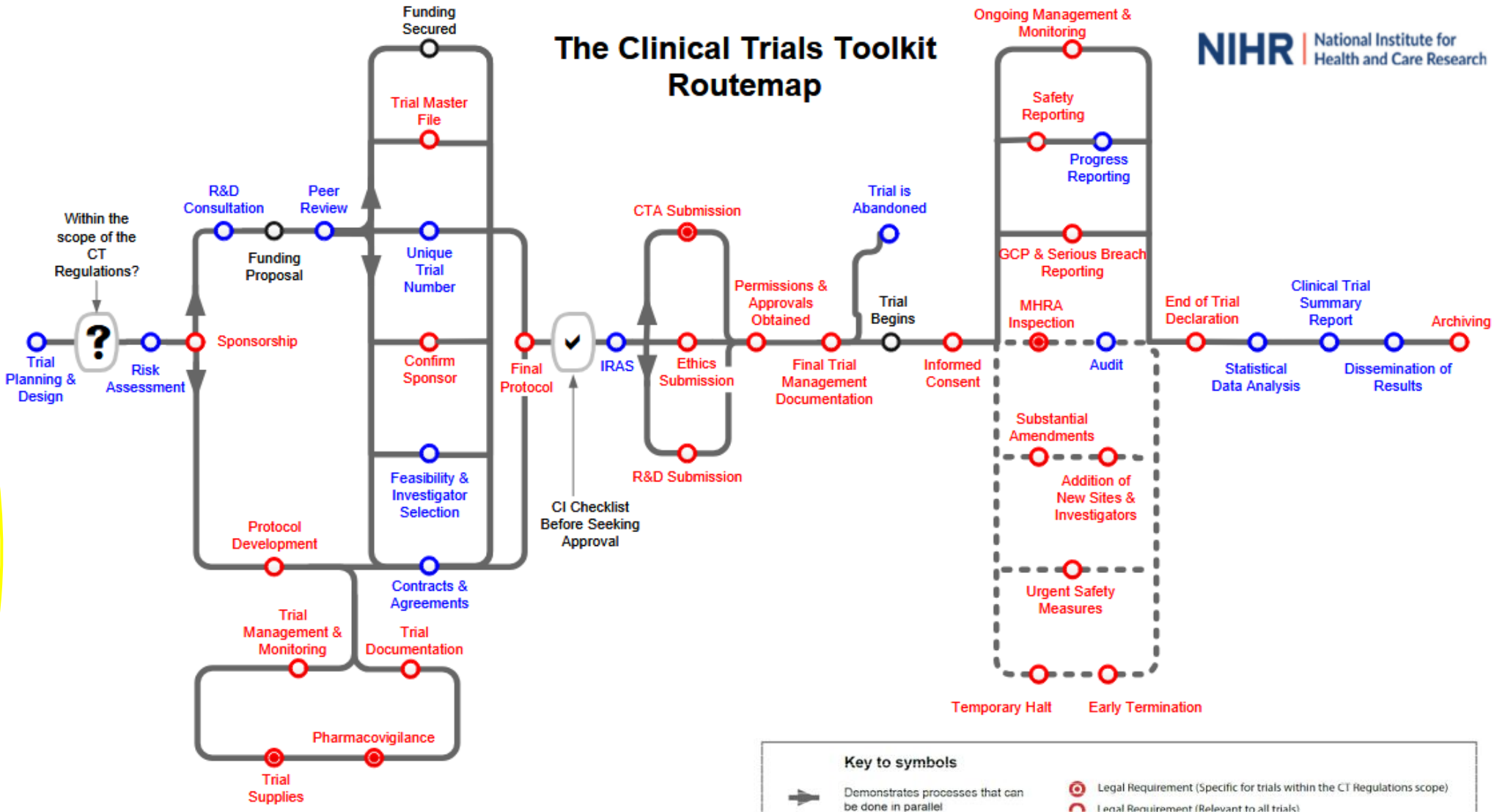
Definitions

Study Life Cycle



https://www.ct-toolkit.ac.uk/routemap

PROJECT

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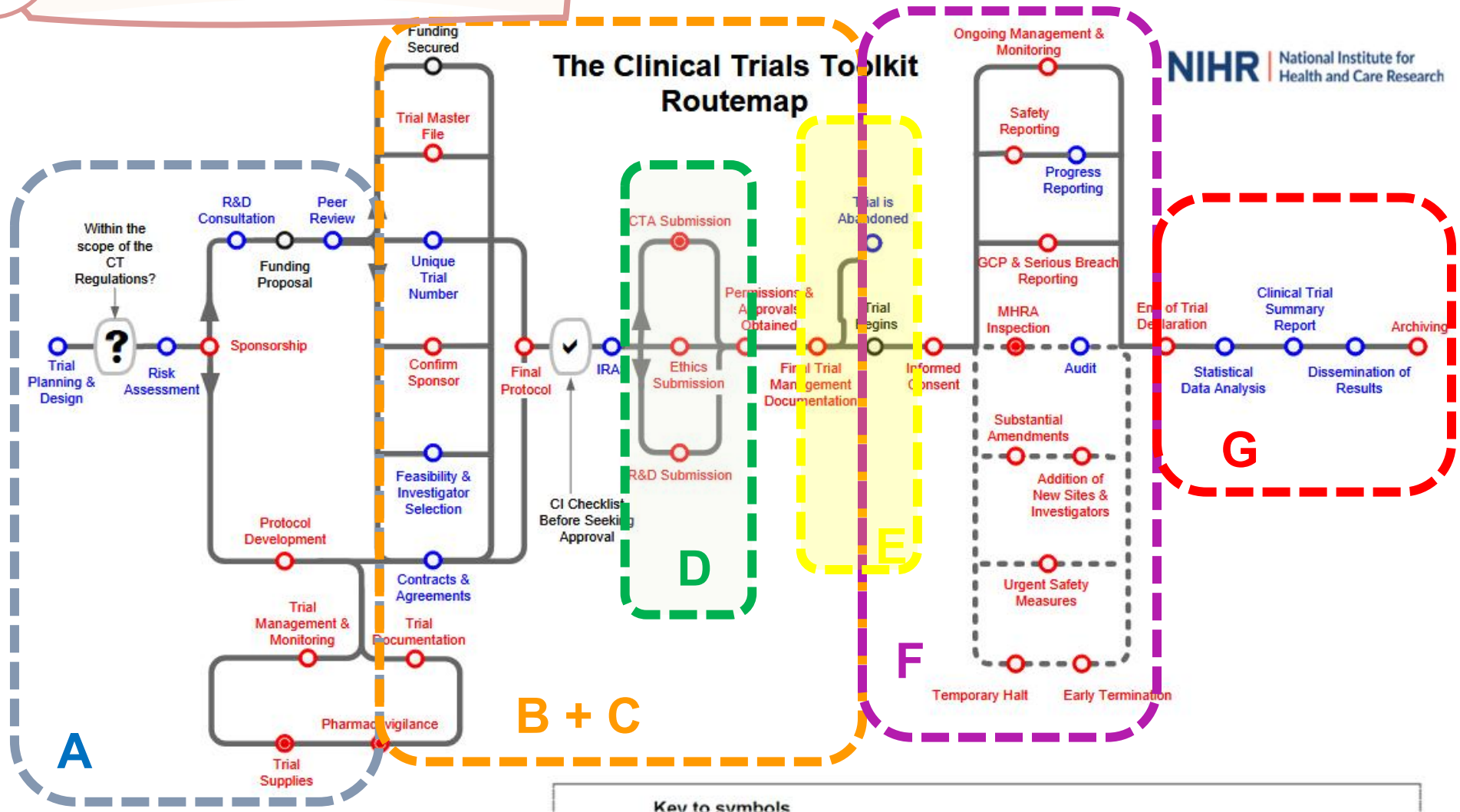
Definitions

Study Life Cycle

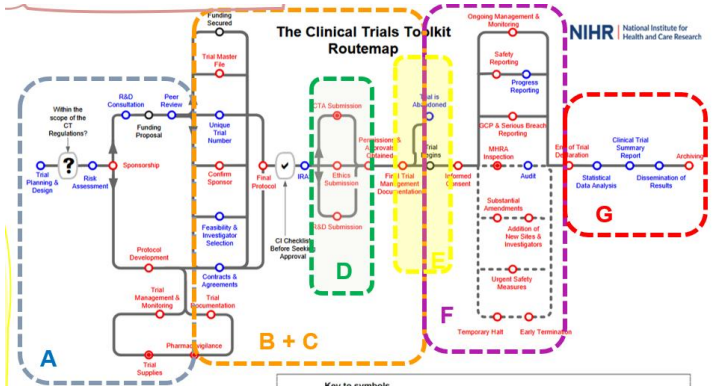


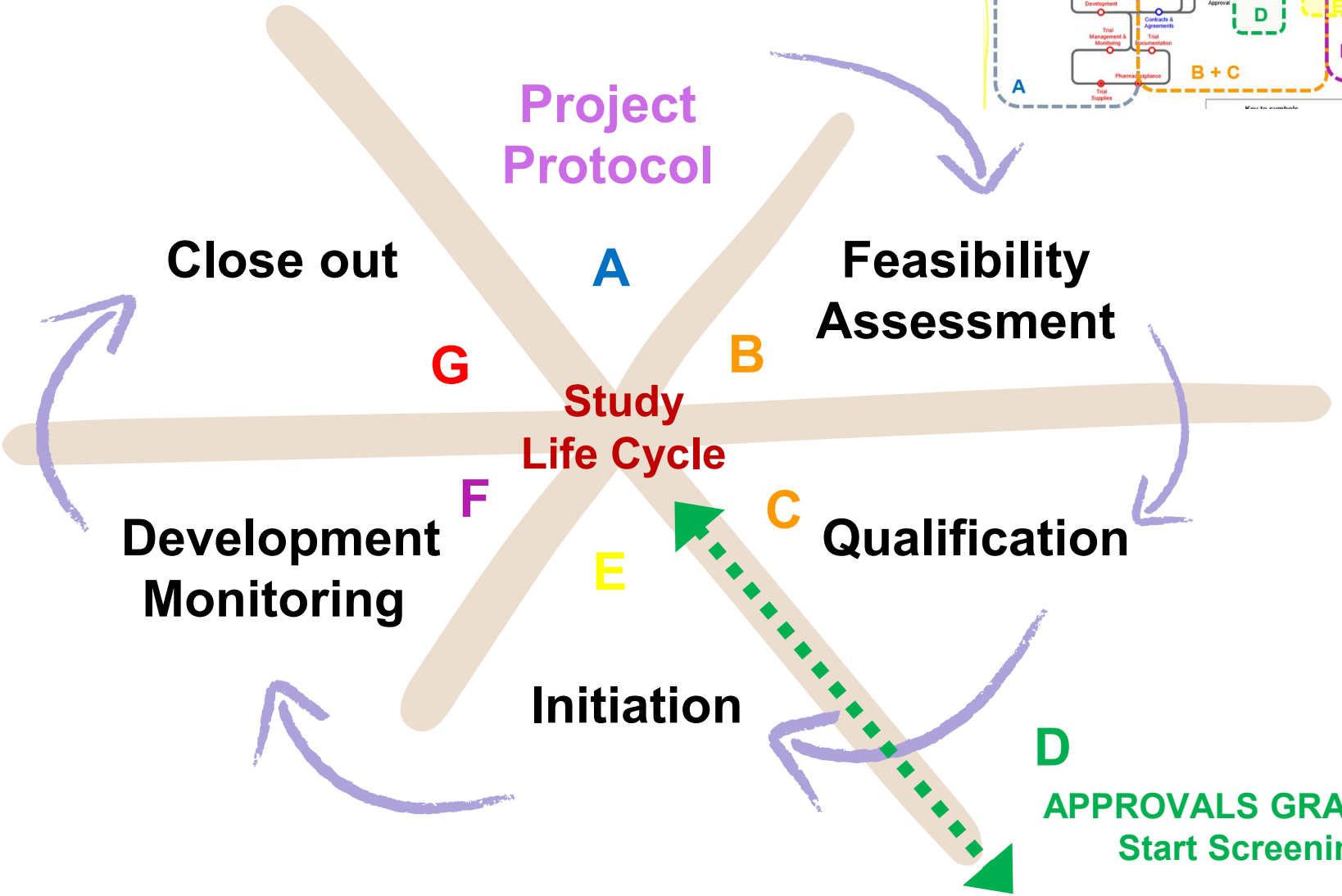
https://www.ct-toolkit.ac.uk/routemap

PROJECT

Definitions

Study Life Cycle





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Definitions

Study Life Cycle

Clinical research project devided into two “stages”:

Planning

Includes identifying the problem; reviewing literature; developing a research question; formulating a hypothesis; determining the type of study; selecting a study design; identifying the target/study population; establishing collaborations with experts and determining the overall feasibility of the proposed work including, data collection strategy, sampling techniques, statistical analysis and the appropriate method to implement the study.

ACTION

“Contact with Sites”; Includes the actionable research, implementation of the method in coherence with the theoretical concept, randomisation, blinding, application of sampling techniques, data collection and statistical analysis.

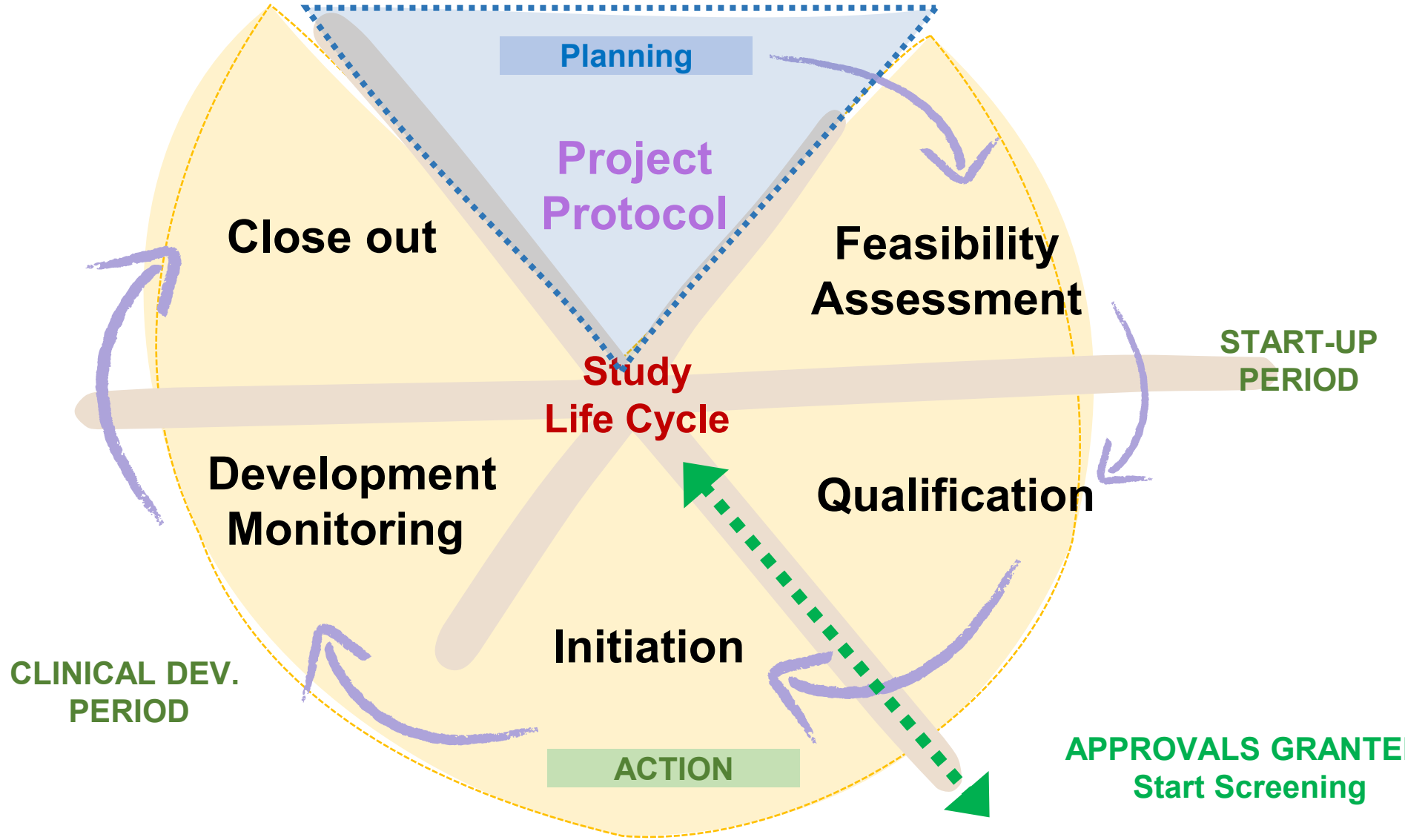
4.3 ICH E6(R3) There should be periodic review of current scientific knowledge and approaches to determine whether modifications to the trial are needed, since new or unanticipated information may arise once the trial has begun.

https://pmc.ncbi.nlm.nih.gov/articles/PMC9710407/pdf/jpmh-2022-02-e267.pdf

PROJECT

Definitions

Study Life Cycle



PROJECT

Definitions

Study Life Cycle

Clinical research project devided according to its “approval status”:

Pre-Approval “Start-up”

Includes the study planning stage and early activities (action stage) such as evaluation of country and site feasibility/qualification; preparation and submission of study and sites for Regulatory and Ethical Evaluation/Approval. All trials go through an approval process. A trial can't begin to recruit, until all approvals are complete.

Study Approval

Pre-stantartized and organized process that consists in the review of the Study Protocol by Regulatory Authorities and Research Ethics Committee, to ensure rights, safety, dignity and wellbeing of Study Participants, before its recruitment. Only, and if, all requirements/criteria are met, study/site is approved.

https://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/how-clinical-trials-are-planned-and-organised/how-clinical-trials-are-approved

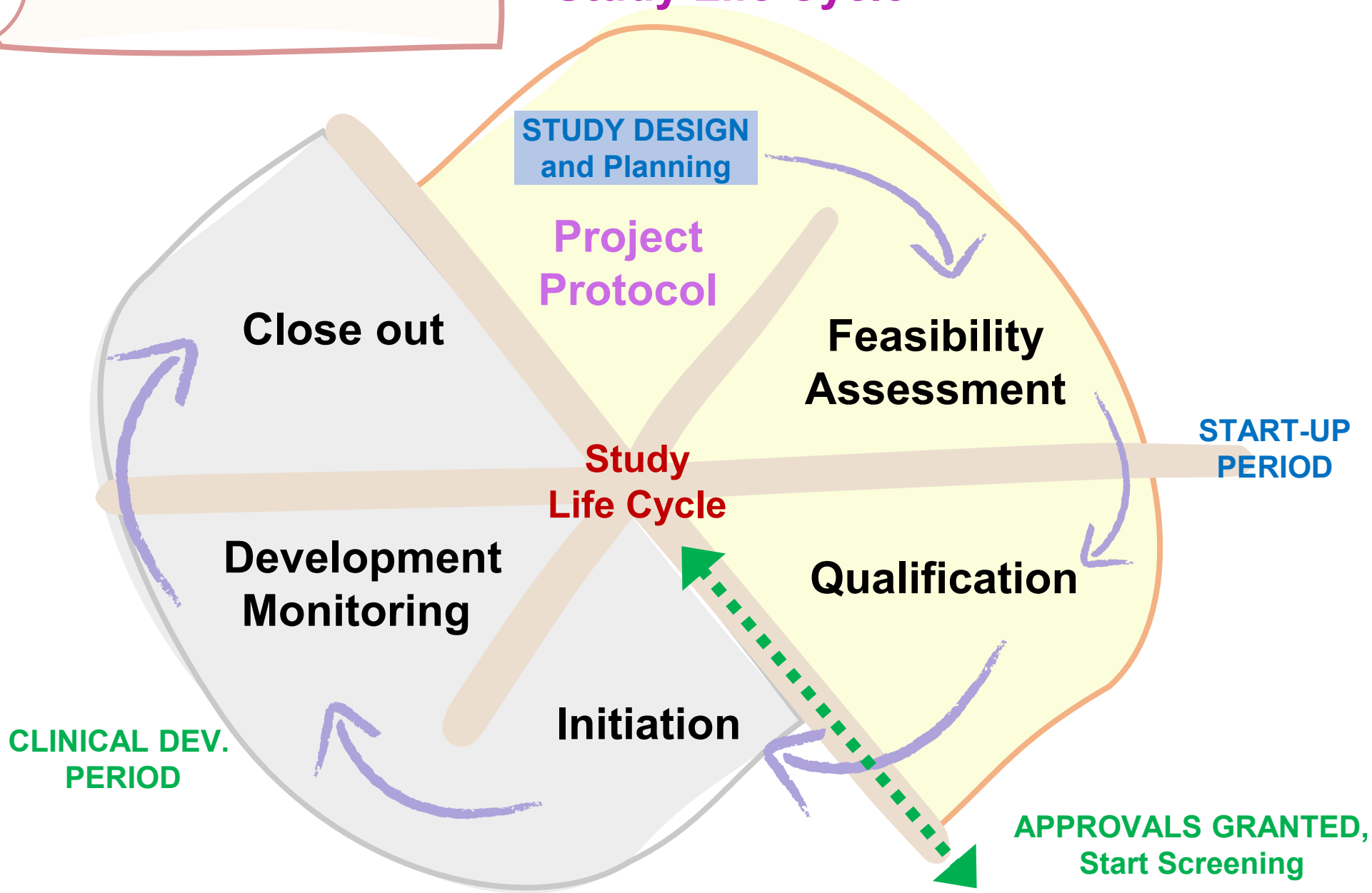
Post-Aproval “Clinical Development”

Includes the study action stage activities related to Study Initiation, Participant’s recruitment; study monitoring stages until study close-out activities. Periodic review of the trial by the IRB/IEC should also be conducted in accordance with applicable regulatory requirements.

PROJECT

Definitions

Study Life Cycle



PROJECT

Definitions

Study Life Cycle

Placing the "**Essential Elements Matrix**"
within the study lifecycle

Critical role in the capacity for continuous and **effective risk assessment and management**

PROJECT

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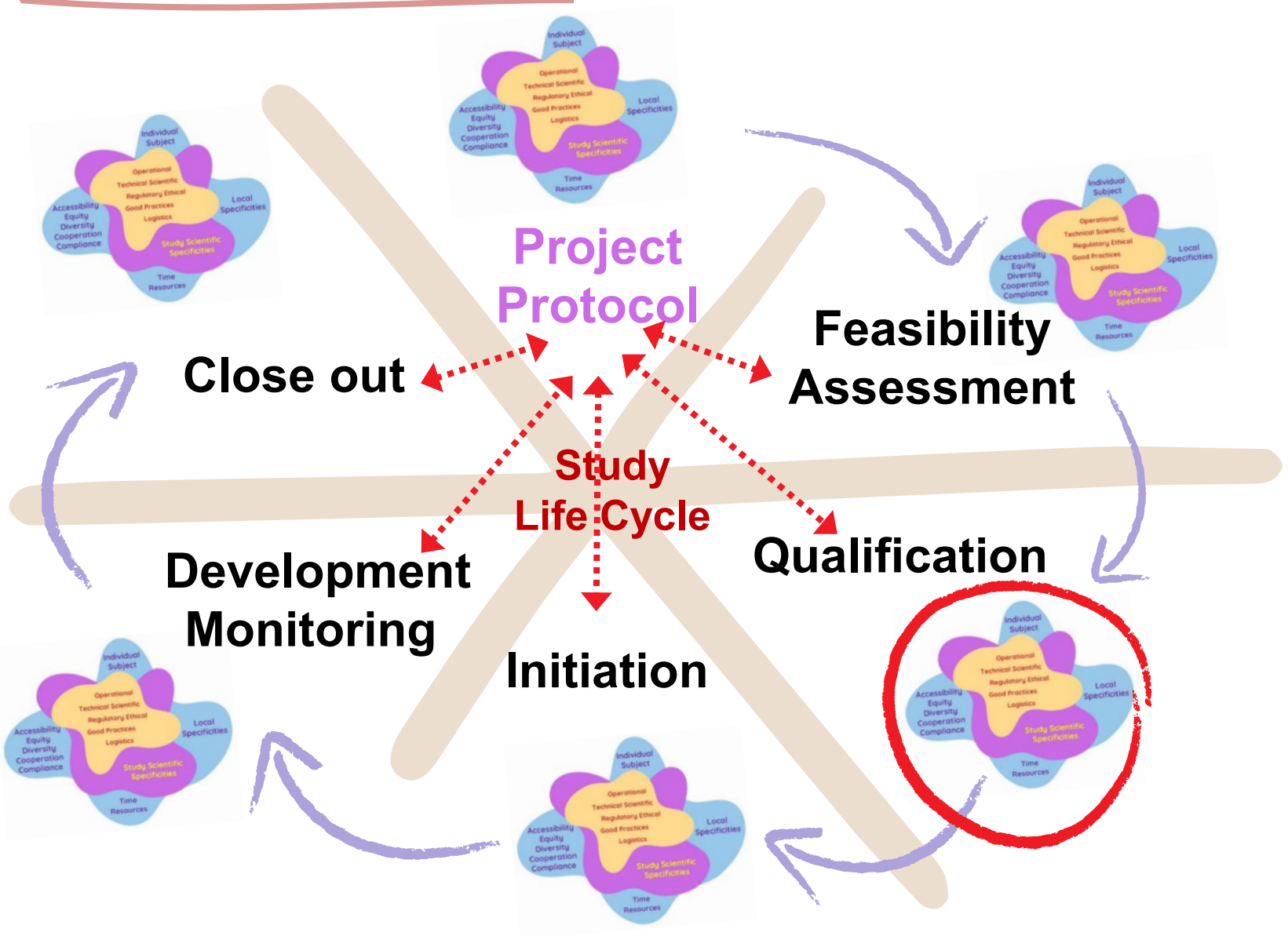
Definitions

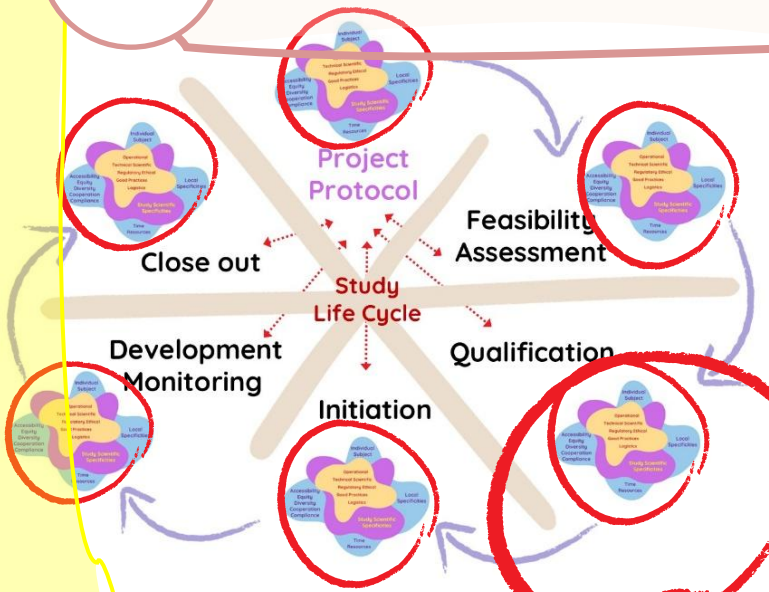
Study Life Cycle



Overview of Essential Elements Matrix at each step of a study lifecycle

PROJECT

Definitions



The Adaptability and dynamism of the projects, protocols, and planned activities result from the ability to respond to new information, including that accessed also during real-world and local Implementation context.

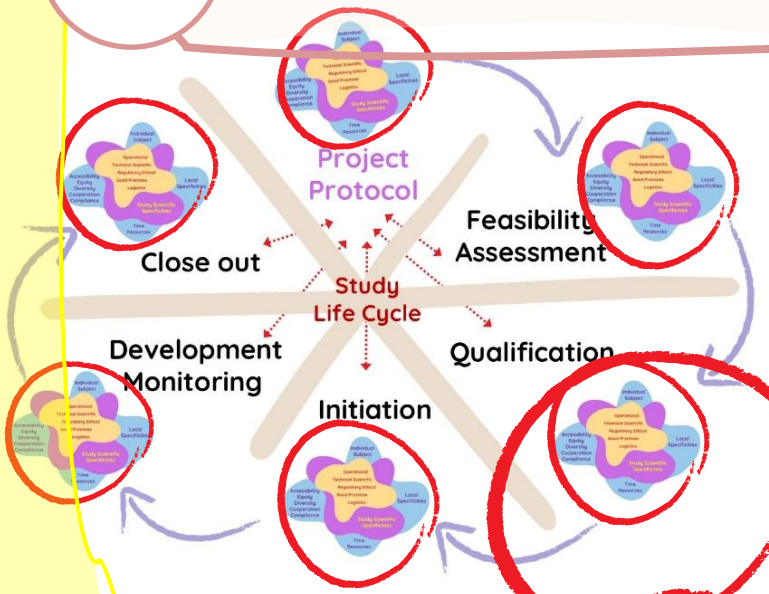
Study Life Cycle

ICH E6(R3)

- ✓ Clinical trials vary widely in scale, complexity and cost. Careful evaluation of critical to quality factors involved in each trial and the risks associated with these factors will help ensure efficiency by focusing on activities critical to achieving the trial objectives.
- ✓ 4.3. There should be periodic review of current scientific knowledge and approaches to determine whether modifications to the trial are needed, since new or unanticipated information may arise once the trial has begun.
- ✓ The responsibility of the sponsor entails the implementation of risk-proportionate approaches to ensure the rights, safety and well-being of the trial participants and the reliability of the trial results throughout the clinical trial life cycle.
- ✓ **Risk-based and proportionate approach to the conduct of a clinical trial.**

PROJECT

Definitions



The Adaptability and dynamism of the projects, protocols, and planned activities result from the ability to respond to new information, including that accessed also during real-world and local Implementation context.

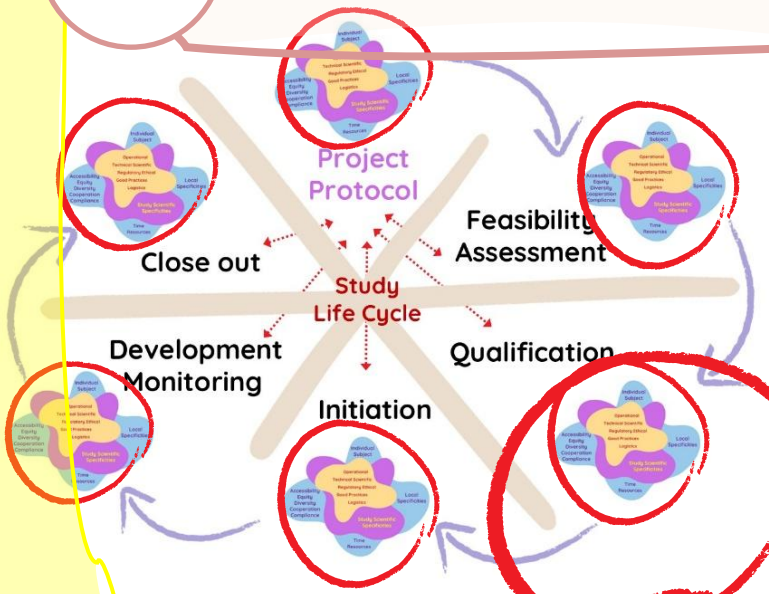
Study Life Cycle

ICH E6(R3)

✓ Quality should be built into the scientific and operational design and conduct of clinical trials. 6.1 6.2 6.3 Quality of a clinical trial is considered in this guideline as fitness for purpose. Factors critical to the quality of the trial should be identified prospectively. These factors are attributes of a trial that are fundamental to the protection of participants, the reliability and interpretability of the trial results and the decisions made based on those trial results. (…) Clinical trial processes, measures and approaches should be implemented in a way that is proportionate to the risks to participants and to the importance of the data collected and that avoids unnecessary burden on participants and investigators.

PROJECT

Definitions



The Adaptability and dynamism of the projects, protocols, and planned activities result from the ability to respond to new information, including that accessed also during real-world and local Implementation context.

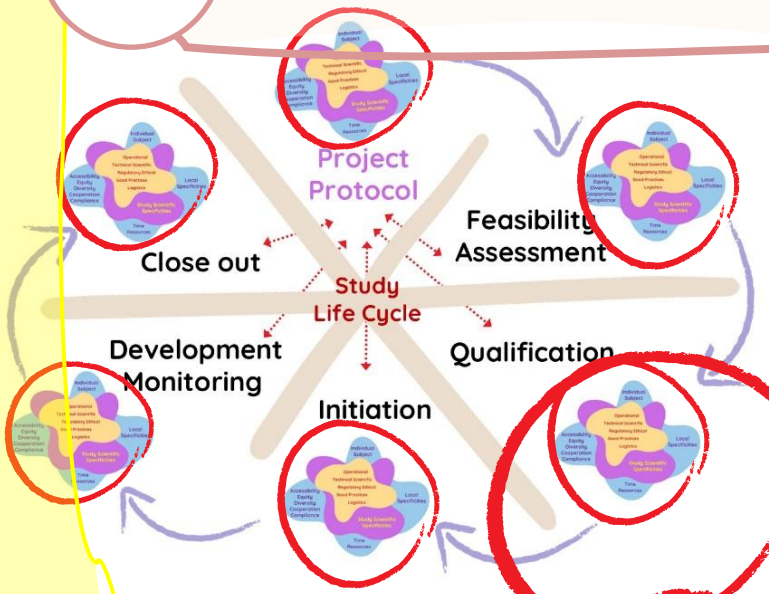
Study Life Cycle

ICH E6(R3)

✓ 7.4 Trial processes should be proportionate to the risks inherent in the trial and the importance of the information collected. Risks in this context include risks to the rights, safety and well-being of trial participants as well as risks to the reliability of the trial results. The focus should be on the risks associated with trial participation. For clinical trials involving patients, the focus should be on risks that go beyond those associated with usual medical care. The risks relating to investigational products that have a marketing authorisation when used in the clinical trial context may differ from the usual care of patients and should be taken into consideration. Risks to critical to quality factors should be managed proactively and adjusted when new or unanticipated issues arise once the trial has begun.

PROJECT

Definitions



The Adaptability and dynamism of the projects, protocols, and planned activities result from the ability to respond to new information, including that accessed also during real-world and local Implementation context.

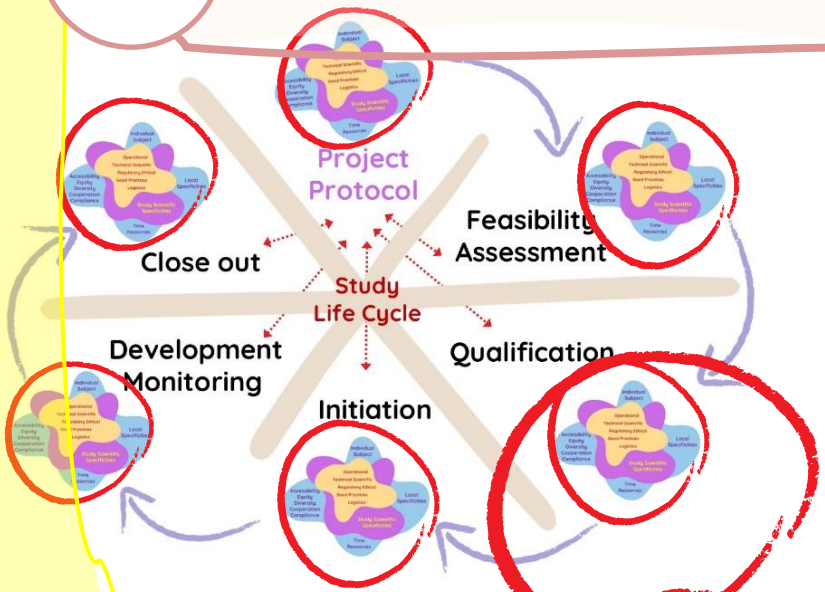
Study Life Cycle

ICH E6(R3)

✓ The Principles of GCP are designed to be flexible and applicable to a broad range of clinical trials. This guideline, along with ICH E8(R1), encourages thoughtful consideration and planning to address specific and potentially unique aspects of an individual clinical trial. This includes evaluation of trial characteristics, such as the design elements, the investigational product being evaluated, the medical condition being addressed, the characteristics of the participants, the setting in which the clinical trial is being conducted, and the type of data being collected. Careful consideration of factors relevant to ensuring trial quality is needed for each clinical trial. The principles are intended to **support efficient approaches to trial design and conduct.**

PROJECT

Definitions



The Adaptability and dynamism of the projects, protocols, and planned activities result from the ability to respond to new information, including that accessed also during real-world and local Implementation context.

Study Life Cycle

ICH E6(R3)

Impact of Trial Quality on Analysis

Differences in trial conduct across regions can negatively have an impact on the power to detect an overall treatment effect, as well as the ability to examine consistency of treatment effects at the analysis stage. Important factors having an impact on the quality of the trial, such as follow-up of study subjects, should be managed consistently across regions, and issues identified during the trial should be corrected as early as possible.

During the conduct of an MRCT, trial monitoring and blinded data review may uncover various issues that require modifications be made to the analysis plan for the trial. For example, for better assessment, it might be necessary in an MRCT to modify pooling strategies for regions or subpopulations, which were carefully defined during trial planning, after sufficient data have been accumulated on the baseline characteristics (e.g., intrinsic and extrinsic factors) of the multiregional population. However, such changes should be justified, discussed with the relevant regulatory authorities, and carried out in a way that preserves trial integrity.

E17 General Principles for Planning and Design of Multi-Regional Clinical Trials | FDA

PROJECT

Definitions

Dynamic “Study IMPLEMENTATION”
↔ **Dynamic** “EXISTING CONTEXT”

The Dynamic “EXISTING CONTEXT” in which the study is developed

Direct CONTEXT

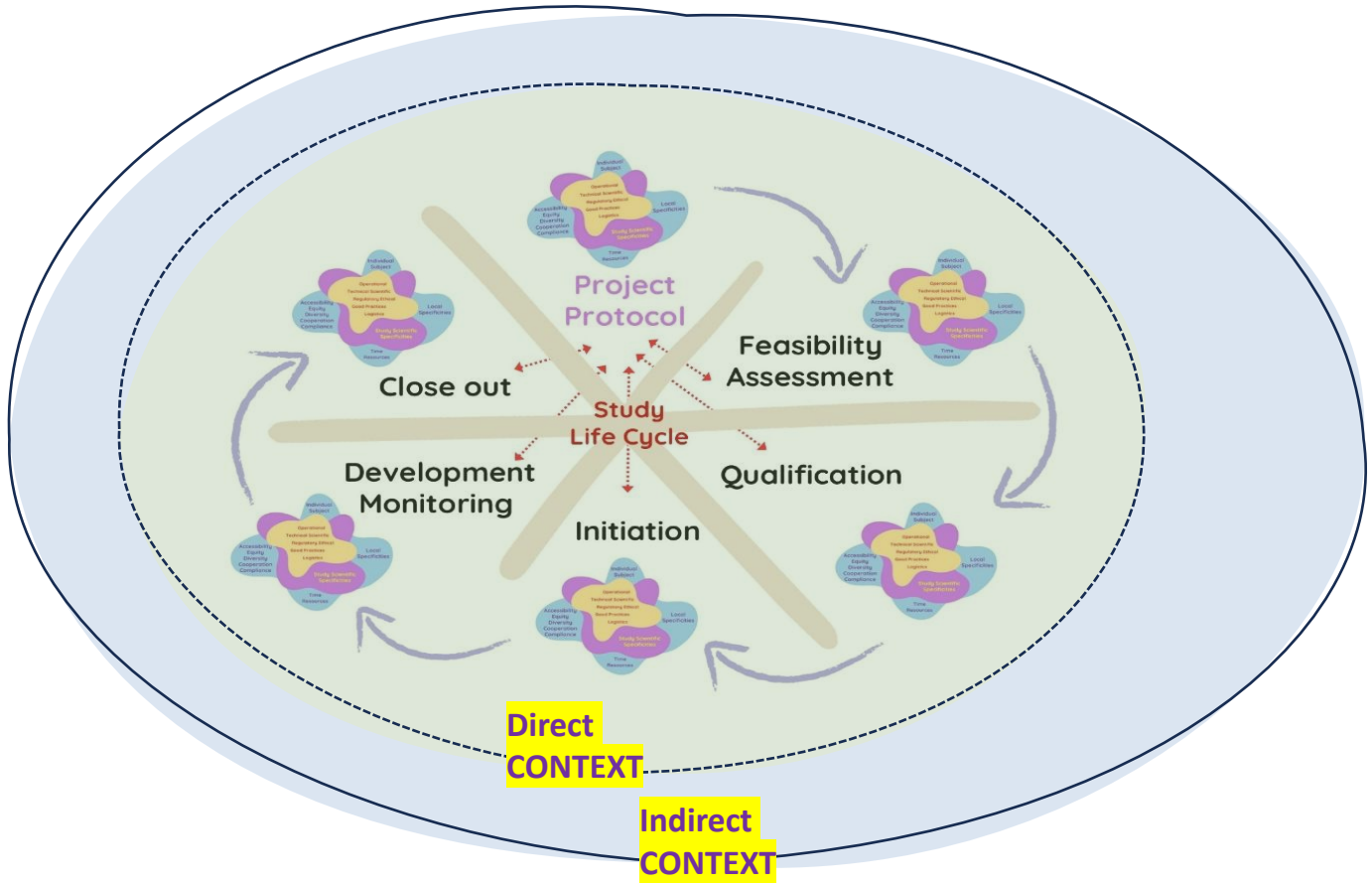
“Study space” context

The immediate environment, knowledge ***“State-of-art”***, setting, or conditionsin which the study is designed and implemented.

Indirect CONTEXT:

“space” outside the study context

External factors or environments, science knowledge fields, not directly involved or related to the study but still potentially influencing it.



PROJECT

Definitions

Dynamic “Study IMPLEMENTATION”
↔ **Dynamic** “EXISTING CONTEXT”

✓ **Context influences the study and the study influences the context**

Direct CONTEXT

“Study space” context

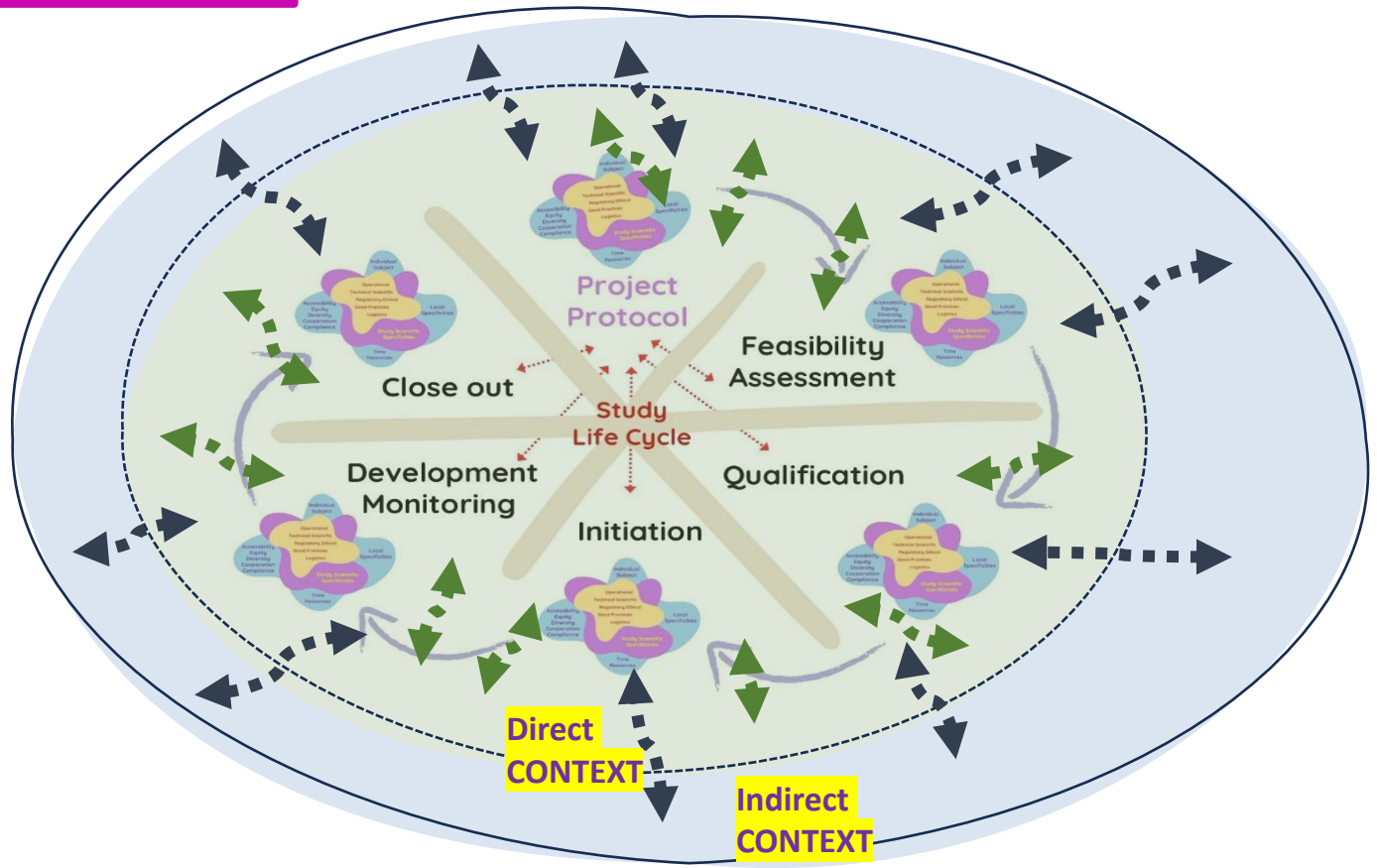
Indirect CONTEXT:

“space” outside the study context

Factors or new Information from the direct study CONTEXT that could affect the study.

Factors or new Information from the indirect CONTEXT that could affect the study.

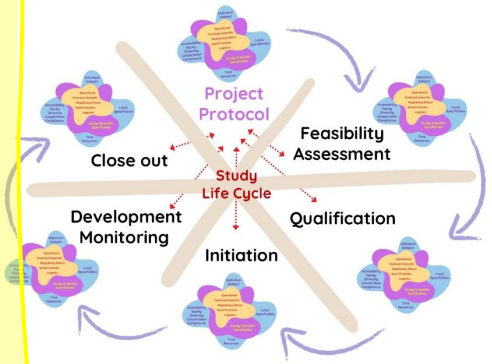
Processes or pathways within the study that enable effective detection, assessment and integration of new information, supporting adequate adaptation throughout all phases of the study life cycle.



PROJECT

Definitions

Study Life Cycle



New Information → Refers to unanticipated information that may arise after the trial has been planned or begun.

Quality Risk Assessment

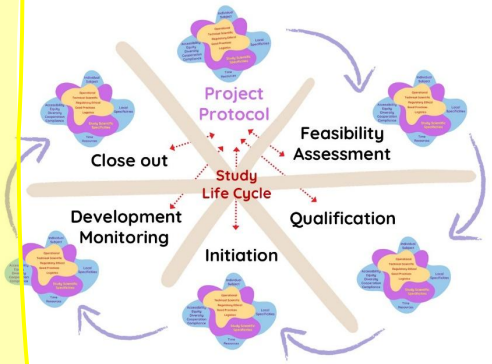
To determine whether it is associated with a hazard that poses a high risk to the safety, rights, or well-being of study participants, or that may significantly affect or modify the study's risk-benefit assessment, scientific or quality validity, procedures, or documentation.

Changes or modifications made to the research project after the initial approval(s) are designated as amendments. Examples of substantial and non-substantial amendments - Health Research Authority

PROJECT

Definitions

Study Life Cycle



New Information: Refers to unanticipated information that may arise after the trial has been planned or begun.

→ **Origin:**

- ✓ Within the study context
- ✓ Outside the study context

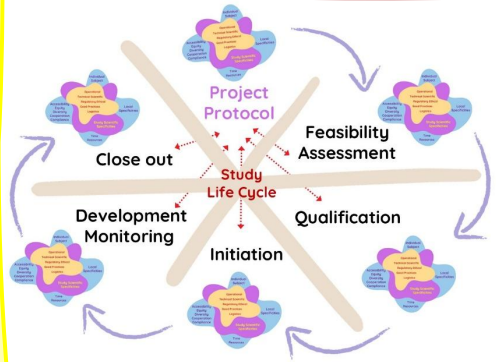
→ **Relevance to the study:**

- ✓ Relevant
- ✓ Non-Relevant

Note: It is important to have the capacity to effectively access the most current, accurate, and complete information across all stages and contexts of study. Often, new information is simply existing data that was not properly identified or recognized earlier.

PROJECT

Definitions



*****Study systems or planed analysis mechanisms:**

- **Pharmacovigilance**
- **Data Monitoring Committee (DMC)**
- **Safety Monitoring Board**
- **Regular safety meetings site Invs and study medical team;**
- **Risk Review Meetings; CAPA, root cause analysis;**
- **Interim analysis;**
- **Annual Progress Reports;**
- **Protocol Deviations Assessment;**
- **Monitoring, Auditing/Inspection.**

Study Life Cycle

New information → Origin

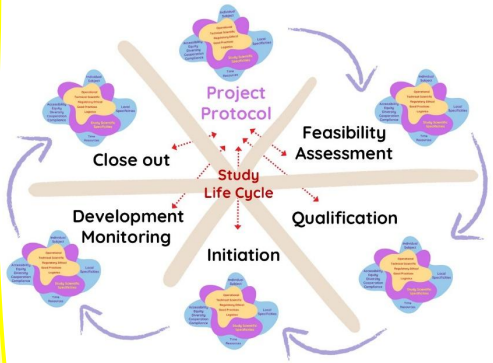
✓ **Within the Study Context**

- New information from the direct study context:
- Resulting from study systems/planed analysis of the accumulated knowledge: interim data analysis, protocol deviations; monitoring visits***, such as Safety Unexpected or unknown adverse events in participants (SUSARs);
- Participant-Reported Information: New data affecting Participant eligibility (e.g. new diagnoses, non-compliance).
- Study Drug Manufacturing: Issues in production, supply, quality, or formulation.
- Reported by sites: changes in site personnel, equipment, procedures, facilities or vendors;
- Scientific-related community: new knowledge from same study field, related studies or experiments;
- Any other: misconduct reporting.

PROJECT

Definitions

Study Life Cycle



New information → Origin

✓ **Outside the Study Context**

New Information from the external context, not study related:

- Political Instability, War, Pandemics, Climate Events: Disruptions to site operations, participant access, or safety.
- Unrelated Scientific/Technological Developments: Innovations outside the study's field that may influence infrastructure, regulations, or technology use.
- Sponsor Strategy or Business Changes: Organizational decisions such as budget changes, restructuring, or project reprioritization.

PROJECT

Definitions

Study Life Cycle

New Information → Relevance to the study:

✓ Relevant

Any new information, regardless of its origin, that is associated with a hazard posing a high risk to the safety, rights, or well-being of study participants, or that may significantly modify the study's risk-benefit assessment, scientific validity, procedures or documents.

Any resulting consequences or changes to the study or its participants must be submitted to the CEC/CA for assessment as a substantial amendment, and/or as a protocol violation/deviation, as applicable.

✓ Non-Relevant

Any new information, regardless of its origin, that is not associated with a hazard posing a high risk to participant safety, rights, or well-being, nor significantly modifying the study's risk-benefit assessment, scientific validity, procedures or documents.

Any resulting consequences or changes to the study must be submitted to the CEC/CA the CEC/CA for assessment as non-substantial.

PROJECT

Definitions

Study Life Cycle

Examples of substantial and non-substantial amendments - Health Research Authority

Examples of substantial amendments:

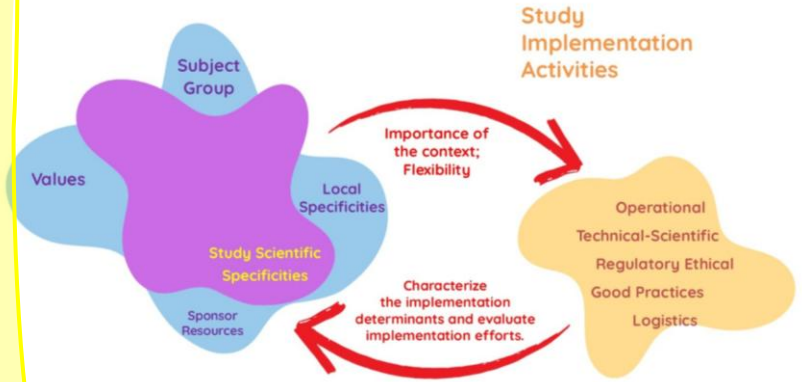
- Changes to the design or methodology of the study, or to background information likely to have a significant impact on its scientific value;
- changes to the procedures undertaken by participants;
- changes likely to have a significant impact on the safety or physical or mental integrity of participants, or to the risk/benefit assessment for the study;
- significant changes to study documentation such as participant information sheets, consent forms, questionnaires, letters of invitation, letters to GPs or other clinicians;
- a change of sponsor(s) or sponsor's legal representative;
- a change to the insurance or indemnity arrangements for the study;
- temporary halt of a study to protect participants from harm, and the planned restart of a study following a temporary halt;
- a change to the definition of the end of the study.

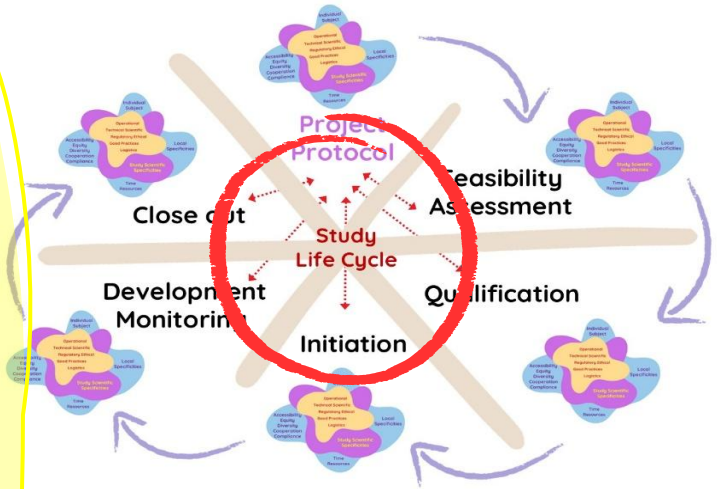
Examples of non-substantial amendments:

- minor changes to the protocol or other study documentation, e.g. correcting errors, updating contact points, minor clarifications;
- updates of the investigator's brochure (unless there is a change to the risk/benefit assessment for the trial);
- changes to the chief investigator's research team;
- changes in funding arrangements;
- changes in the documentation used by the research team for recording study data;
- changes in the logistical arrangements for storing or transporting samples;

PROJECT

Definitions





Study Planning, implementation and monitoring (tools Identification and management of new information)

Dynamic "Study IMPLEMENTATION" ↔

Dynamic "EXISTING CONTEXT"

✓ **"continuous assessment of the risk-benefit balance"**

Processes or pathways that enable continuous and effective identification assessment and integration of new information

Technical-Scientific	Study Protocol and Plans
Regulatory-Ethical	Global, Country, Site Regulatory (legal) and Ethical Requirements for Research
Guidelines-Good Practices	ICH Guidelines

Adequate Study Adaptation

Research under continuous EC/CA safeguarding and oversight, ensuring that is conducted ethically, with rigorous scientific standards, proper safety and high-quality.

PROJECT

INVpath

Definitions

Study Life Cycle

Key Considerations for Designing More Effective Evaluation of New Information and Risk Assessment Throughout the Study Lifecycle:

Data Sharing

- New studies should be designed and planned based on the most comprehensive and up-to-date knowledge, strategies, and tools/technologies (Scientific validity, Operational feasibility, Safety concerns, Ethical considerations). Variations in study planning and selected tools, required to be more finely tailored to each therapeutic area and study complexity → further research and models required.

- It is crucial to have/be able to incorporate data from scientific literature, regulatory guidance and updates, safety data from related studies and emerging real-world evidence data related to the local context, populations, and communities where studies are being conducted. This allows more accurate and realistic evaluation of the conditions under which the studies will take place.

- Enables the development of more effective strategies to identify and manage emerging information that may pose risks to participants or study integrity (Prevention/Harm Reduction).

PROJECT

INVpath

Definitions

Study Life Cycle

Key Considerations for Designing More Effective Evaluation of New Information and Risk Assessment Throughout the Study Lifecycle:

Efficient Reporting and Communication Systems (Role of AI)

- Implement lighter, faster and universal capture, reporting/communication and evaluating systems—potentially leveraging artificial intelligence (AI).
- These systems should be accessible to all study team members, clinical sites, stakeholders and regulatory/ethics committees (CE/RA) and reduce amendments/changes evaluation efforts;
- Capable of supporting faster reporting, better data characterization, enhanced follow-up (FUP) and documentation/sharring of risk assessment processes at all levels;
- Designed to enable timely (real-time) identification of appropriate actions to protect participants and ensure compliance. (Mitigation/Risk Minimization)

PROJECT

INVpath

Definitions

Study Life Cycle

Key Considerations for Designing More Effective Evaluation of New Information and Risk Assessment Throughout the Study Lifecycle:

Assertive Training of Study Teams

✓ **Provide comprehensive training for all study team members on:**

- **Study design and scientific/medical background,**
- **Operational systems and procedures,**
- **Local context and implementation challenges.**

✓ **This training enhances individual and team capabilities in:**

- **Identifying, assessing, and managing new information,**
- **Understanding causes and potential risks/consequences,**
- **Planning and executing corrective and preventive actions effectively.**

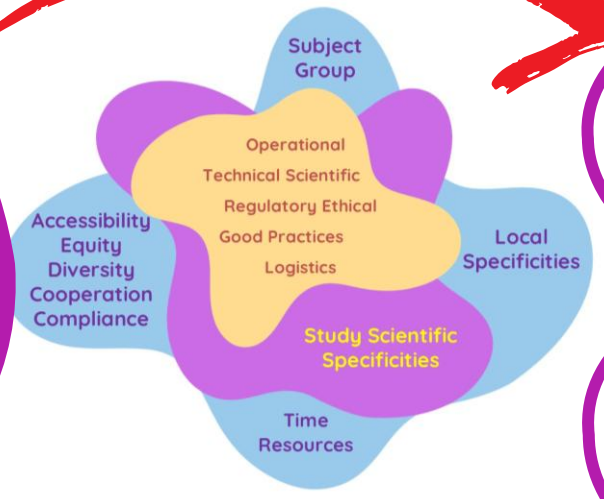
(Harm Reduction and Risk Minimization)

PROJECT

Activities

Study Implementation Activities

Support the Local Development, Implementation and Monitoring of Human Health Research, Clinical Research studies, promoted by Diverse Organizations and Contexts



- Support in the development of study related materials
- Study feasibility assessment and local qualification
- Integration of best practices at local, national, and international levels
- Study submission to CEC/RA
- Study Initiation, monitoring and close-out procedures
- Communication and coordination among all stakeholders
- Maximizing: *Participants wellbeing *Study compliance
- Reducing: *risks *deviations *resources burden

Thank YOU!

Health Development

INVpath

Sílvia Oliveira, Biologist, Clinical Research 2025

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