PREPARING TO RUN A TRIAL

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- **PHASE 1 STUDIES**
- **This phase is designed to assess the safety (pharmacovigilance), tolerability, pharmacokinetics, and pharmacodynamics of a drug.**

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- **STUDY**
- **DESIGN**

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- **Phase I clinical trials are an essential step in the development of anticancer drugs. The main goal of these studies is to establish the recommended dose and/or schedule of new drugs or drug combinations for phase II trials.**
- **Dose Escalation Scheme: The guiding principle for dose escalation in phase I trials is to avoid exposing too many patients to subtherapeutic doses while preserving safety and maintaining rapid accrual**
- **Traditional 3+3 design: Cohorts of three patients; the first cohort is treated at a starting dose that is considered to be safe and the subsequent cohorts are treated at increasing dose levels that have been fixed in advance**
- **Rule-Based Designs: These designs comprise the so-called "up-and-down" designs because they allow dose escalation and de-escalation. The general principle of this design is to escalate or de-escalate the dose with diminishing fractions of the preceding dose depending on the absence or presence of severe toxicity in the previous cohort of treated patients**

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- **Accelerated Titration Designs** Accelerated titration designs combine features from variations of the traditional 3+3 design and the model-based design.
- **Pharmacologically Guided Dose Escalation:** The PGDE method is another variation of the traditional 3+3 design that has not been widely used in clinical practice
- **Model-Based Designs:** An alternative dose escalation method for phase I clinical trials is to use statistical models that actively seek a dose level that produces a prespecified probability of dose-limiting toxicity by using toxicity data

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Clinical Trials Submissions

- **INVOLVING:**
  - Sponsor (& Chief Investigator)
  - MHRA (Clinical Trial Authorisation for IMPs)
  - NHS Research Ethics Committees (NRES) (ethical approval)
  - Sheffield Teaching Hospitals NHS Trust Research & Development Department (local Trust approval)
  - CCTC Clinical Trials Executive (CTE)
  - WPH Clinical Services Group - Clinical Director
  - CCTC Clinical Trials Administration

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INTERACTIVE SESSION

Clinical Trials submission pathway (1):

- Peer review complete
- Protocol & associated documents finalised
- Trial Management & Monitoring arranged
- Secured funding
- Pharmacovigilance procedures finalised
- Trial supplies/drug available
- Unique trial number (EudraCT number) obtained
- Trial Master File set up

→ Sponsor applies for Clinical Trial Authorisation from MHRA

Clinical Trial Authorisation granted

Sponsor submits NHS REC application

Sponsor notified of favourable ethical opinion from main REC

Sponsor sends trial information (e.g. protocol) to potential PI at WPH

ECMC

Clinical Trials submission pathway (2):

Trial discussed & approved by CCTC Clinical Trials Executive

Trial approved by Clinical Services Group & signed off by Clinical Director

CCTC coordinator registers trial with STH R&D department

CCTC cordinator submits Site Specific Information form to STH R&D

Approvals & signatures required:
MHRA CTA
Main REC Approval
SSI form
STH Finance
UoS Finance
UoS Insurance
Data Protection
Laboratories
Pathology
Imaging
Pharmacist
Physicist
Radiation Protection (ARSAC)

Clinical Trials submission pathway (3):

All obtained approvals, signatures and SSI plus the following documents:
Investigator brochure
Protocol
Patient Information Sheets
Consent Forms
Quality of Life Forms
Study worksheets
GP letter/information sheet
Curriculum vitae (PI)

→ CCTC coordinator submits to STH R&D for research governance approval and NHS permission

Financial agreements and contracts signed by UoS and STH as necessary

STH director of research issues clinical trial authorisation letter to PI

STUDY OPEN TO RECRUITMENT

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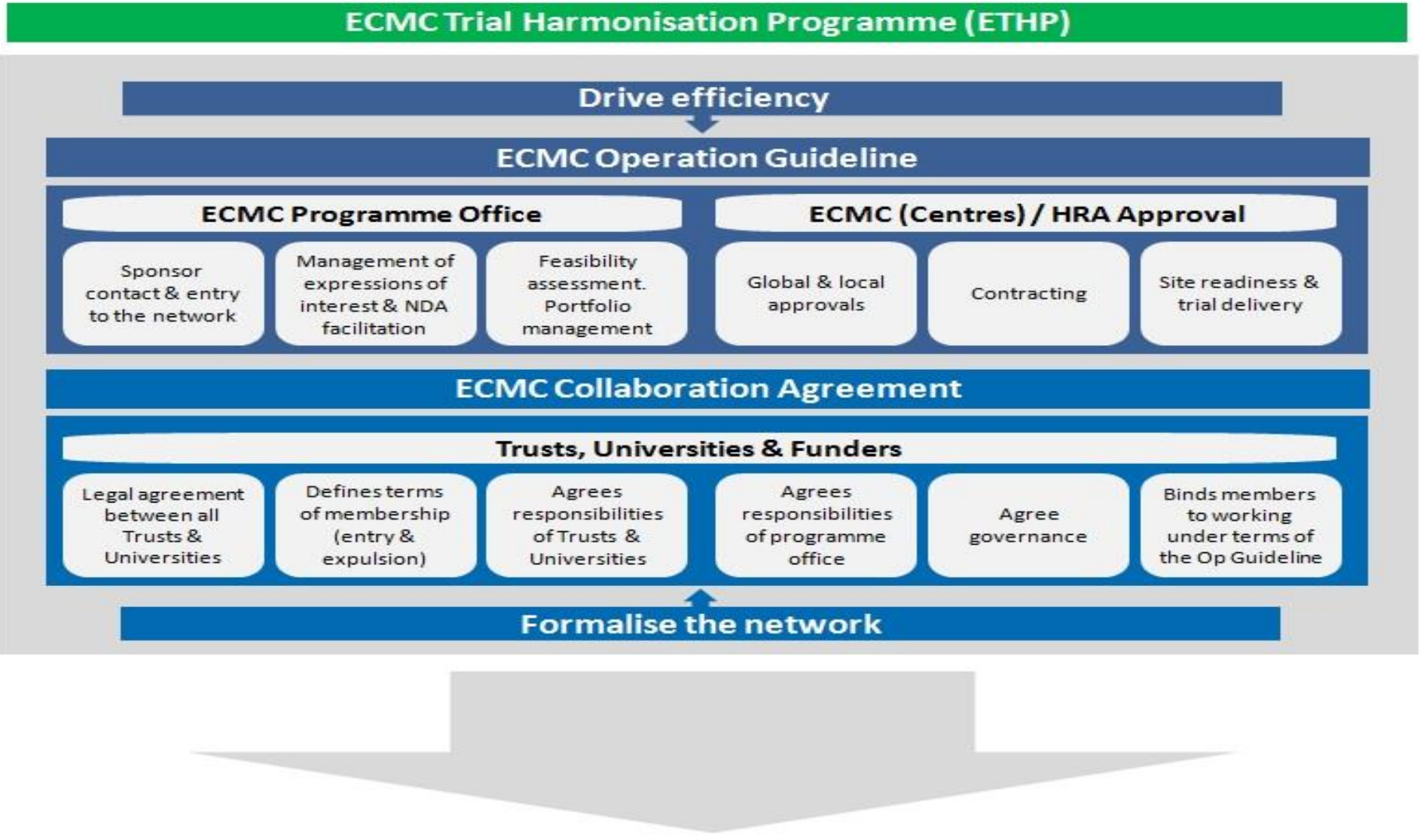
- **ECMC Trial Harmonisation:** The ECMC Trial Harmonisation Programme (ETHP) aims to help build on the current ECMC initiative and transform it into a UK-wide, world-class Network for the fast and efficient delivery of early phase oncology clinical trials. The research infrastructure of the ECMC initiative makes it ideally placed to harmonise this process and transform the way UK-wide early phase cancer trials are managed across the Network.



- Active portfolio and performance management
- Shorter trial set up times
- All locations legally obliged to work to agreed standards
- Nimble partnership – membership can change

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- SITE FILE MANAGEMENT
- Site SOP for Investigator Site File management
- Examples of Site File index

Food for thought

- **Patient numbers**
  - -Total Number of patients
  - -Number of patients per year
- **Date expected trial to start and finish**
  - -How will you manage patient workload
  - -is it a high intensity trial
  - -
- **Length of planed treatment**
  - -6 cycles
  - -Until progression

Patient.

- **Patient population**

  -are your patient numbers realistic?

- **How will you get referrals,**

  - screen clinics, referrals, MTD

  -posters, email, news letters

- **What is the frequency of each day case visit?**

  - 3 weekly.

  - Weekly

Treatment

- Bed /chair space
- How much “chair time” for each treatment
- Date expected to complete
- Length of planed treatment
- **Safety bloods same day as treatment**

Staff

- Enough qualified staff to work on study
- Who will do what
- Do you need specific training
- Is the trial labour intensive
- Are there 14hr PK days
- Who will staff unit out of hours

Equipment

- **Protocol requirements**

- Trial ECG who will service/repare
- Certain type of monitoring equipment
- Calibration / Certificates
- Cost
- Storage
- For trial use only

Pharmacy

- Staff
- Who will supply IMP
- Storage
- Documentation
- Short expiry time
- How long will it take to make drug,
- Randomization
- Patient numbers can pharmacy supply for 3 pt in one day?

Radiology

- Ring fenced slots
- CT/ MRI waiting list how much notice
- Muga Echo, ARSAC
- Reporting
- ***If unable to secure slots***
- Plan B ?
- Out source, cost
- SLA

Departments

- **Who do you need?**
- Ophthalmology?
- Cardiology?

- Who needs to be on delegation log/ how will this be managed if these services are on different sites

Training

- GCP
- Complex blood sampling
- IMP given in non standard way
- Trial specific equipment
- ECRF who how long. Time
- IVRS who need more that 1
- Time lines