NATIONAL OFFICE FOR RESEARCH ETHICS COMMITTEES

CTR Implementation: National Office Perspectives

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HRB NCTO International Clinical Trials Day

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NATIONAL OFFICE FOR RESEARCH ETHICS COMMITTEES

*'Ethics is knowing the difference between what you have a right to do and what **is** right to do'*

Potter Stewart

National Office for Research Ethics Committees

- Independent office with statutory role
- Hosts and facilitates the work of National Research Ethics Committees (NREC)
- Mission to embed a robust, transparent & cohesive research ethics review system that strengthens national research infrastructure
- NRECs assembled in prescribed areas of health research over time by Head of National Office and appointed by Minister for Health
- NRECs have been established for:
  - Clinical Trials for Investigational Medicinal Products (NREC-CT, two Committees)
  - Clinical Investigations of Medical Devices (NREC-MD)
  - Covid-19 (NREC-Covid-19)
  - Covid-19 Biobank (NICB REC)
- NRECs provide a single national ethics opinion on applications and substantial modifications

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VISION

Ireland's system of research ethics review cultivates the benefits of health research for patients and the public.

MISSION

The National Office will embed a robust, transparent and cohesive research ethics review system that strengthens the national research infrastructure.

STRATEGIC PRIORITIES

01 **To deliver a robust and transparent system** for NRECs that provides competent and timely ethics review.

02 **To partner with health research stakeholders** with the mutual objective of ensuring that Ireland's ethics review framework is poised to adopt international best-practice and change.

03 **To engage with the research ethics committees community**, researchers and the wider public to facilitate education on ethical decision-making.

04 **To be a thought-leader in the research ethics arena** by seeding discussion, advancing debate, and providing trusted information.

05 **To be an agile and trusted office** in national public service.

NREC-CT Structure

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	NREC-CT A B
Scope	**Clinical Trials of Investigational Medicinal Products CTR**
Membership	28 members each for A & B
Meeting Frequency	Two main meetings per month, up to two subcommittee meetings per month
Reporting	Minister for Health
Operational Support	National Office
Remit	New clinical trial applications, substantial modifications

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Clinical Trial Regulation (EU)

CTR National Implementation

- Decision for Member State to delineate roles in Part I and Part II assessment (i.e. HPRA / NREC-CT) to reach single national decision;
- NREC role and composition remains national decision; need to comply with CTR procedure and timelines.

Clinical Trial Regulation
Timeline

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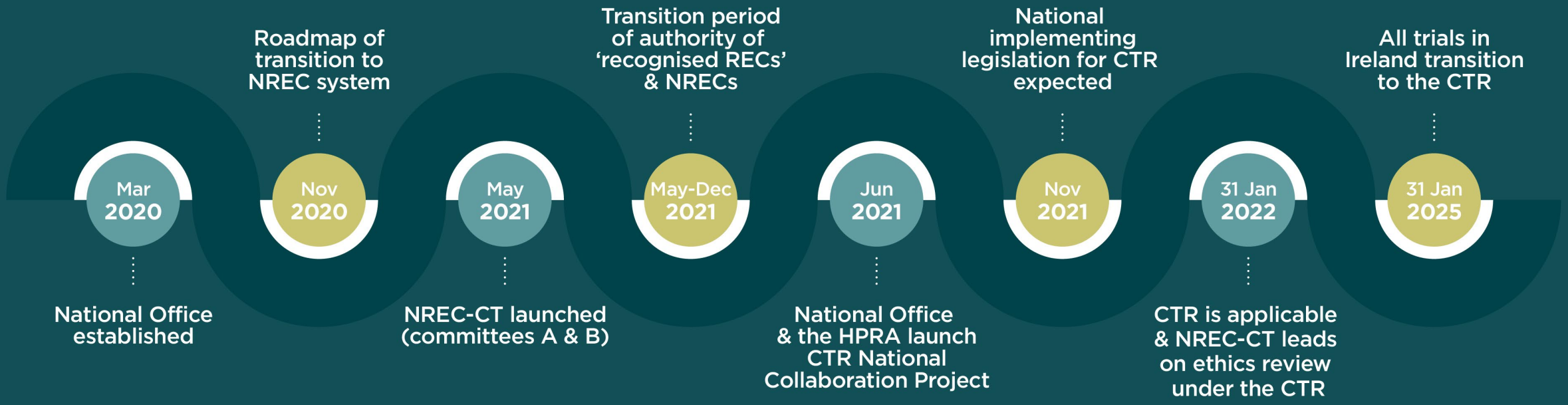

CTR Clinical Trial Regulation
HPRA Health Products Regulatory Authority
NREC(s) National Research Ethics Committee(s)
NREC-CT National Research Ethics Committee for Clinical Trials of Investigational Medicinal Products
REC(s) Research Ethics Committee(s)

nrecoffice.ie

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Background - Clinical Trials Regulation

- CTR came fully into effect on 31st January 2023, completing the transition period between CTD and CTR
- EU-wide submission, through CTIS
- Documents are submitted in two Dossiers:
  - Part I documents are the same for all member states (MSC), and include the Cover Letter, Protocol, DSMB Charter, IB, Scientific Advice, etc.
  - Part II documents are country-specific, and include all details on recruitment, participant-facing documents, insurance, details on PI and sites, compliance with data and biological sample legislation and compensation for participants

What documents are submitted in the Part II Dossier?

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1. Recruitment arrangements
2. Participant information and informed consent
3. Suitability of investigator
4. Suitability of facilities
5. Proof for insurance and indemnification
6. Financial and other arrangements
7. Collection, storage and use of biological samples
8. Data Protection – Compliance with National Requirements & GDPR

Changes for the NREC-CT

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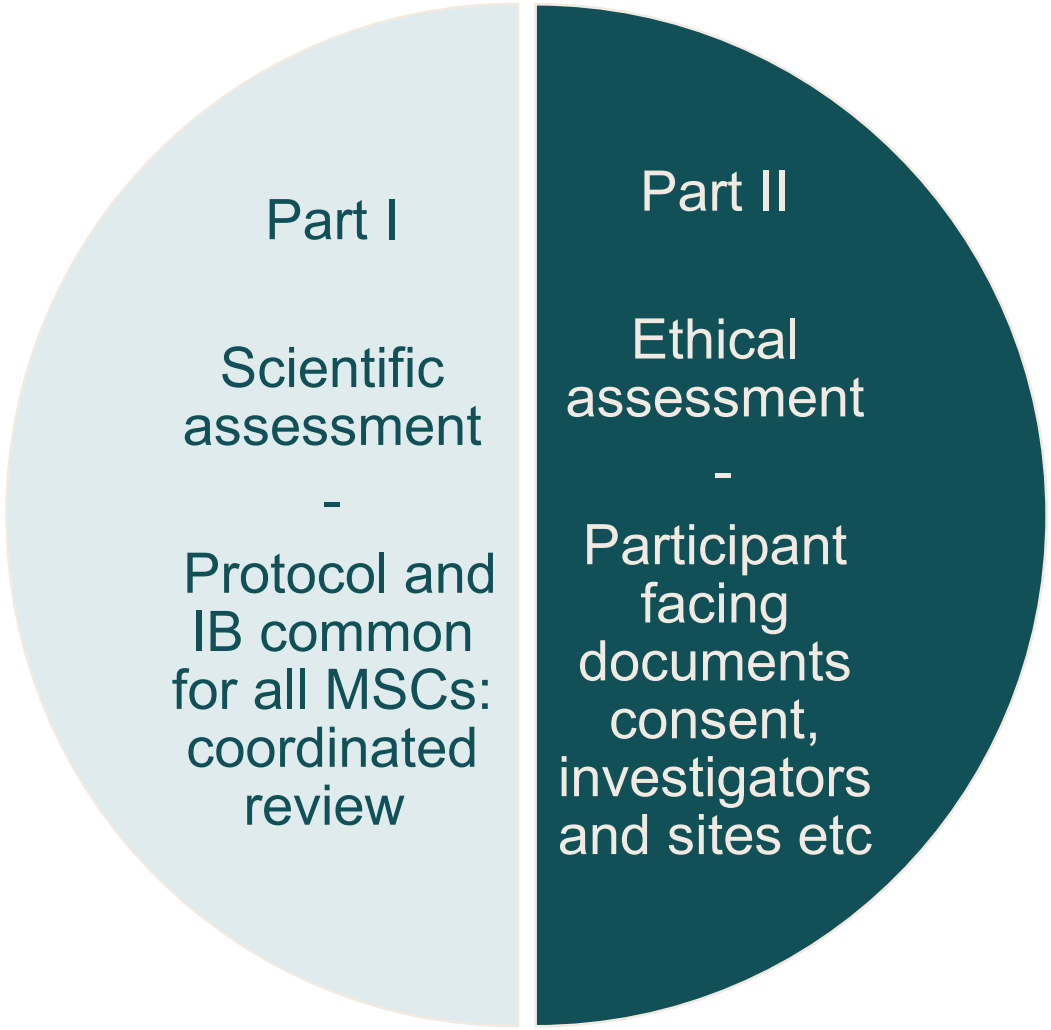

29 new applications

10 substantial amendment

17 transition trials

- Part I and Part II do not need to be submitted together:
  - NREC-CT may be reviewing Part I and Part II separately – potentially 2 years apart
  - No requirement for an applicant to submit a Part II
- NREC-CT will only have one opportunity to request changes or further information under an ‘RFI’ for both Part I and Part II under most circumstances
- Applicant can appeal an NREC-CT decision

Harmonisation Across EU

- Part II requirements, templates and personal data harmonised across member states
  - EMA templates provided, each MSC can also provide own, however must be clear what is optional and what is mandatory
  - Some documents may be different in some MSC due to National law (for example, data protection in IE due to HRR)

- EU Working Groups, Workshops, Roundtables

Benefits identified to date

- One Portal, all tasks completed on one system
- Concrete timelines to work to
- Dossiers are well defined under distinct headings
- Naming convention for documents
- Ease of raising considerations
- Reduction in emails, approval letters
- One RFI reduces amount of time going between review team and applicant
- Harmonisation
- Validation process and RFI mean that trials are much less likely to be invalid for review
- Validation process allows more oversight of what trials are upcoming for review

Issues identified to date

- One RFI (unless in specific circumstances) can hamper completion of RFI response if not satisfactory- risk of refusal is higher
- Limitation of condition definition
- System can have bugs (although recently much better)
- Harmonisation also means that documents that cannot be mandatory, are sometimes still required for full review of trial and must be requested at RFI
- Clarity around addition of MSC after Part I has been completed- role of review
- If Part I only submitted, Investigators not identified which can make it difficult to identify COI for reviewers
- Difficulty in guaranteeing expedited timelines if meeting schedule does not allow an expedited review

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NREC-CT Review Process

NREC review process

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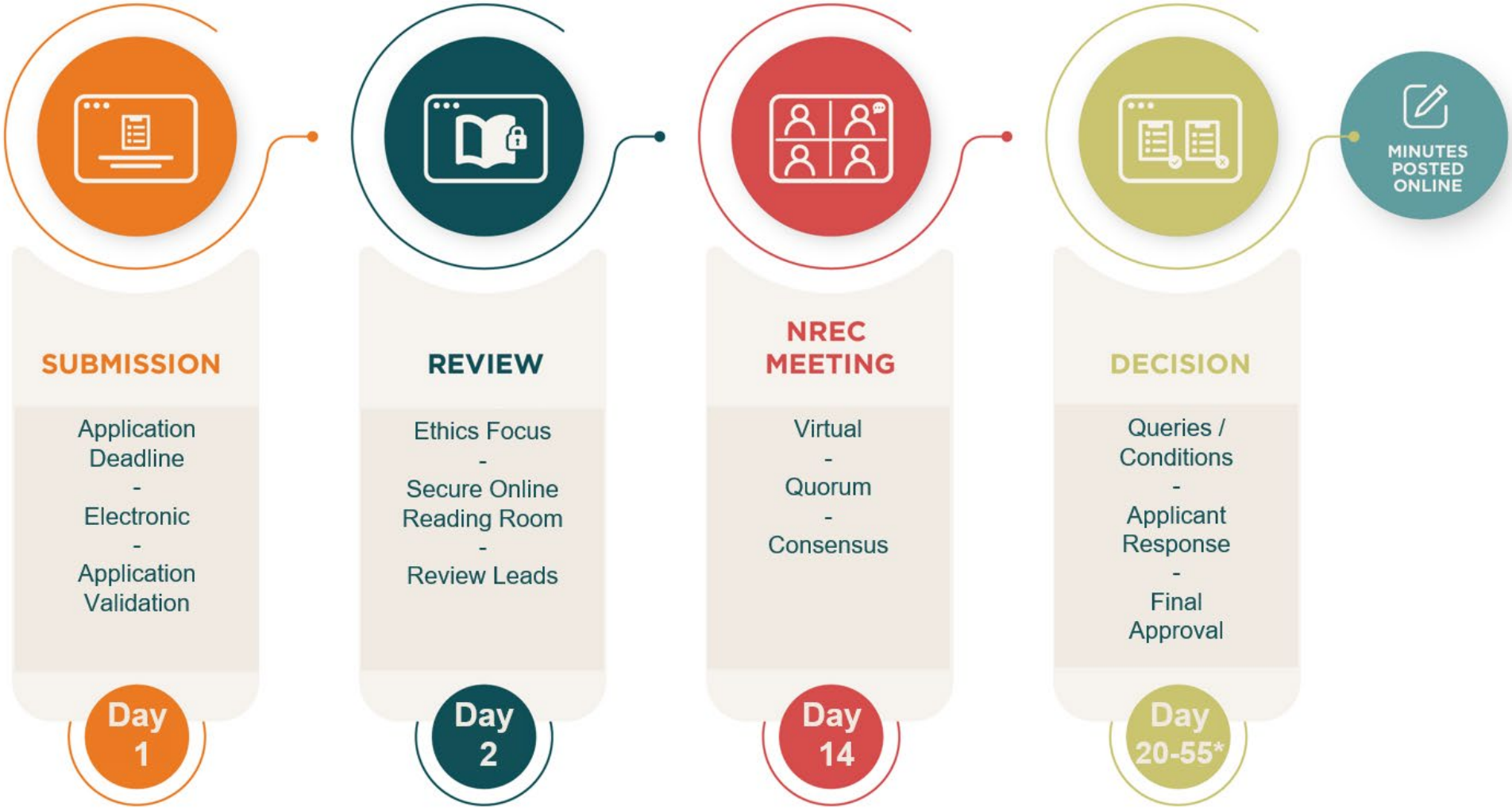
- Similar review format across NRECs
- Timeframe for responses stipulated by European Regulations



Indicative timing by way of example, *20-55/60

Typical NREC considerations

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- **Application documentation**

  e.g. Comprehensively completed in an accessible language

- **Scientific design and conduct of the study**

  e.g. Appropriateness of the study design in relation to study objectives
  Criteria for suspending or terminating research
  Adequacy of the PI and site including support staff, facilities and emergency procedures evidence of relevant experience & training (eg GCP)
  Justification of predictable risks & inconveniences vs anticipated benefits
  Duplicity of / misinformed research effort

- **Recruitment of participants**

  e.g. Initial contact and recruitment
  Inclusion and exclusion criteria (Unjustified exclusion of vulnerable groups?)

- **Care and protection of participants/**

  e.g. Insurance & indemnity agreements
  Financial arrangements, participant compensation

Typical NREC considerations

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- **Protection of confidentiality of participants/volunteers**

  e.g. Extent to which the information will be anonymised

  How long samples/data will be kept

  Security of online tools

  DPIA & DPO input

- **Informed consent process**

  e.g. Comprehensiveness and understandability of written & oral information

  Identification of those responsible for obtaining consent (risk of coercion, power relationships)

  Arrangements for vulnerable participants

  Aligned with Data Protection Act 2018

- **Community considerations**

  e.g. Impact & relevance on the local community and on the concerned communities from which participants/volunteers are drawn

  Description of the availability and affordability of any successful study product to the concerned communities following the research

  Plans to disseminate outcomes

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THANK YOU

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