Health Research Authority

# Capitalising on our experience in the review of early phase clinical trials - Phase I issues from the HRA perspective

**Catherine Blewett**
**HRA Senior Development Manager**
**22 June 2018**

NHS
Health Research Authority

# Scope

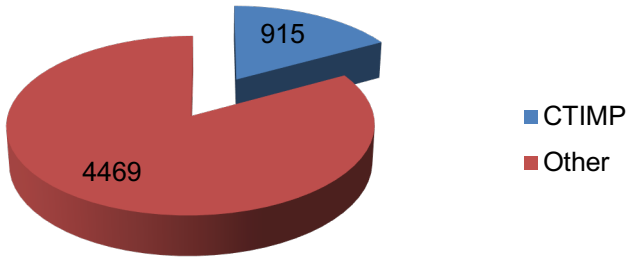
- Phase 1 in the broader context of the HRA / RES
- Initiatives to better facilitate early phase trials
- The future vision for Phase 1

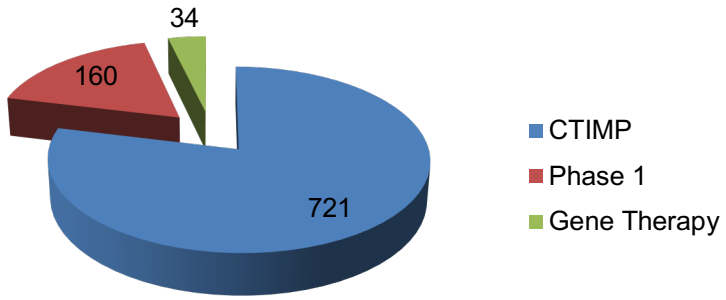
NHS
Health Research Authority

# Phase 1 in the broader context of the HRA / RES

# 1 January 2017 – 31 January 2017

- 5384 applications reviewed
  - CTIMPs 915 (17%) (34 Gene Therapy & 160 Phase 1 - < 1%)
  - Non CTIMP 4469 (83%)



NHS
Health Research Authority

# Comparison year on year

| Year | CTIMP | Phase 1 | Gene Therapy CTIMP |
|---|---|---|---|
| 2012 | 758 | 167 | 16 |
| 2013 | 829 | 186 | 20 |
| 2014 | 762 | 186 | 11 |
| 2015 | 815 | 174 | 18 |
| 2016 | 774 | 168 | 26 |
| 2017 | 915 | 160 | 34 |

NHS
Health Research Authority

# Initiatives to better facilitate early phase trials

# What's most important in early phase trials?

We've been listening …..

- Short and predictable timelines
- Consistency and predictability
- UK being globally competitive
- Having a world class governance infrastructure

Health Research Authority

# Timelines (Phase 1)

- 24 – days – average to issue final opinion (not including the number of days to respond to a provisional opinion) – range 8-58 days
- Usually expect submission same day as booking
  - Have an exception for Phase 1
  - Allow booking up to 7 days before the meeting
- Period from booking to submission – highest 114 days (average 30 days)

Health Research Authority

# Short and predictable timelines

- The quickest route to approval is a favourable opinion after the initial review.
- What you want and what we want is to be able to issue a favourable opinion first time.
  - ‘Getting it right first time’

Health Research Authority

# Short and predictable timelines

- The quickest route to approval is a favourable opinion after the initial review.
- What you want and what we want is to be able to issue a favourable opinion first time.
  - ‘Getting it right first time’

Health Research Authority

# Opinions Issued (Phase 1) - 2017

- Favourable Opinion – 20 (12.5%)
- Favourable Opinion with Conditions – 37 (23%)
- Provisional Opinion – 101 (63%)
- Unfavourable Opinion – 2 (1%)
  - PK data from rats was pending – application therefore considered to be not complete (resubmitted and received FO)
  - Insufficient pre-clinical data – no resubmission

Health Research Authority

# Opinions Issued (Phase 1) - 2017

- Favourable Opinion – 20 (12.5% CTIMP 2%)
- Favourable Opinion with Conditions – 37 (23% CTIMP 15%)
- Provisional Opinion – 101 (63% CTIMP 85%)
- Unfavourable Opinion – 2 (1% CTIMP 2.5%)
  - PK data from rats was pending – application therefore considered to be not complete (resubmitted and received FO)
  - Insufficient pre-clinical data – no resubmission

# What are we doing?

- So what are we doing to achieve this?
  - Have audited reasons for not being able to issue a favourable opinion and will publish soon (similar to the GNAs published by the MHRA).
  - Have developed guidance for staff and members on how to approach requests for changes to they can be addressed as a condition rather than provisional (doesn't require further REC review)
  - Reviewing staff roles to help facilitate the review
  - Protocol templates

Health Research Authority

# Provisional Opinion

Most common

- Changes  required to the participant facing documentation
  - Contraception
  - Info for partner
  - Make clear that first time in human
  - US language in PIS
  - PIS not in easily understandable language

**** A well written and clear information will often mean the difference between a favourable and provisional****

Health Research Authority

# Provisional Opinion

Most common

- Points of clarification
  - Dose escalation
  - Sample size
  - Recruitment strategy

****Describe the trial fully in clear, comprehensive language. Identify the ethical issues and clearly describe how they are being addressed****

Health Research Authority

# Consistency and Predictability

- Challenges
  - Committee system
    - Volunteers
    - Approx 25 RECs review Phase 1 (85 Total)
    - Also review a broad range of other research
  - Timelines
  - Being reactive / keeping up with new innovations which have different ethical issues
  - Complex design structures

Health Research Authority

# What are we doing?

- Shared Ethical Debate
  - Identify areas of inconsistency or differing of opinion
  - Take this forward
    - Training
    - Guidance
    - Individual outliers

Health Research Authority

# What are we doing?

- Consistency Programme
- Phase 1 Advisory Group
  - Brings together REC and Phase 1 community
- Review and approval of generic documents etc.
  - Generic review committee
  - Generic screening template
- Opinion audits
- Comms and training

Health Research Authority

# What are we doing?

- HRA Approval – NHS sites
  - Application to set up < timelines
- Adaptive design trials
  - We know these are important
  - Part of a collaborative working group developing a consensus paper

Health Research Authority

# REC Choice

- Refused First Available
  - 127 yes – 33 no

- Indicates choice is important
  - Could be a challenge in the future
  - Need to focus on consistency and predictability

NHS
Health Research Authority

# The future vision for Phase 1 trials

Health Research Authority

# HRA vision

- Committed to
  - UK being globally competitive and
  - Having a world class governance infrastructure

- We want the UK to be the place to come to deliver world class Phase 1 trials

Health Research Authority

# Communicating UK success

- Not just about being a great place….

  Also about demonstrating the UK is a great place to do early phase clinical trials
- Looking at how we can communicate and support CROs
  - Information on the HRA website
  - Publication of metrics
  - Transparency

NHS
Health Research Authority

# Combined Ways of Working with the MHRA

- Single application to both MHRA and REC
- Co-ordinated review
- Single communication - request for information
- Single communication – confirm final outcome
- Competitive timelines – committed to retaining current Phase 1 timelines

NHS
Health Research Authority

# Thank You