# MHRA Update, March 2022

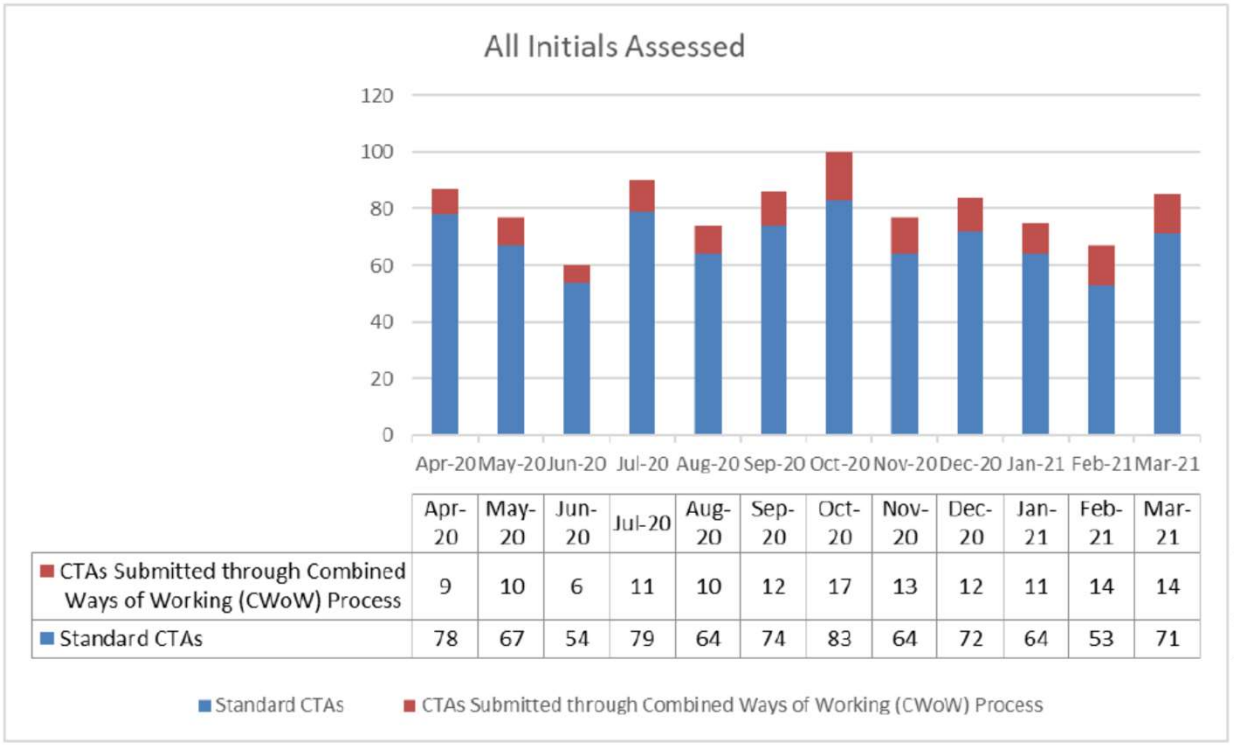
Dr Kirsty Wydenbach, MHRA

# Agenda

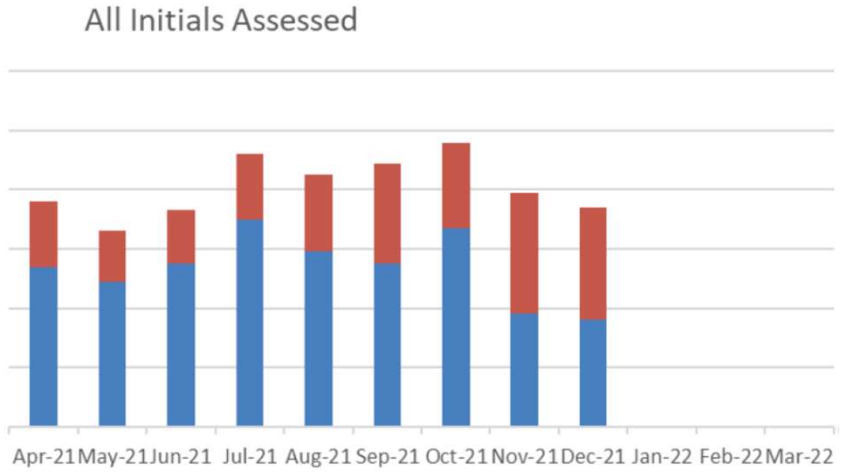
- Metrics, including combined review
- COVID trials
- Combined IMP/device research
- Brief ILAP update
- CTR and impact in UK
- Legislation update

# Metrics

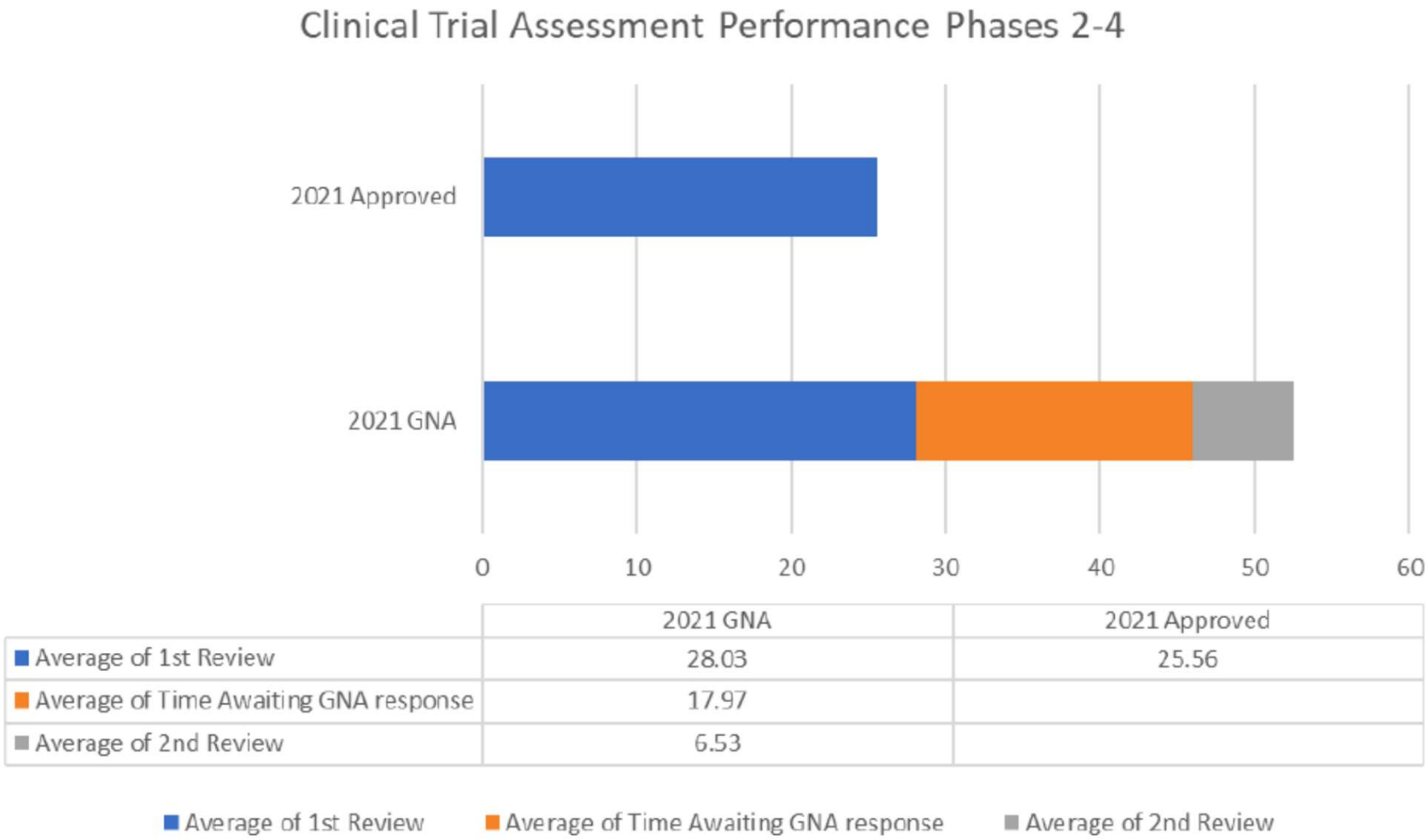
https://www.gov.uk/government/publications/clinical-trials-for-medicines-authorisation-assessment-performance




| | Apr-20 | May-20 | Jun-20 | Jul-20 | Aug-20 | Sep-20 | Oct-20 | Nov-20 | Dec-20 | Jan-21 | Feb-21 | Mar-21 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| CTAs Submitted through Combined Ways of Working (CWoW) Process | 9 | 10 | 6 | 11 | 10 | 12 | 17 | 13 | 12 | 11 | 14 | 14 |
| Standard CTAs | 78 | 67 | 54 | 79 | 64 | 74 | 83 | 64 | 72 | 64 | 53 | 71 |

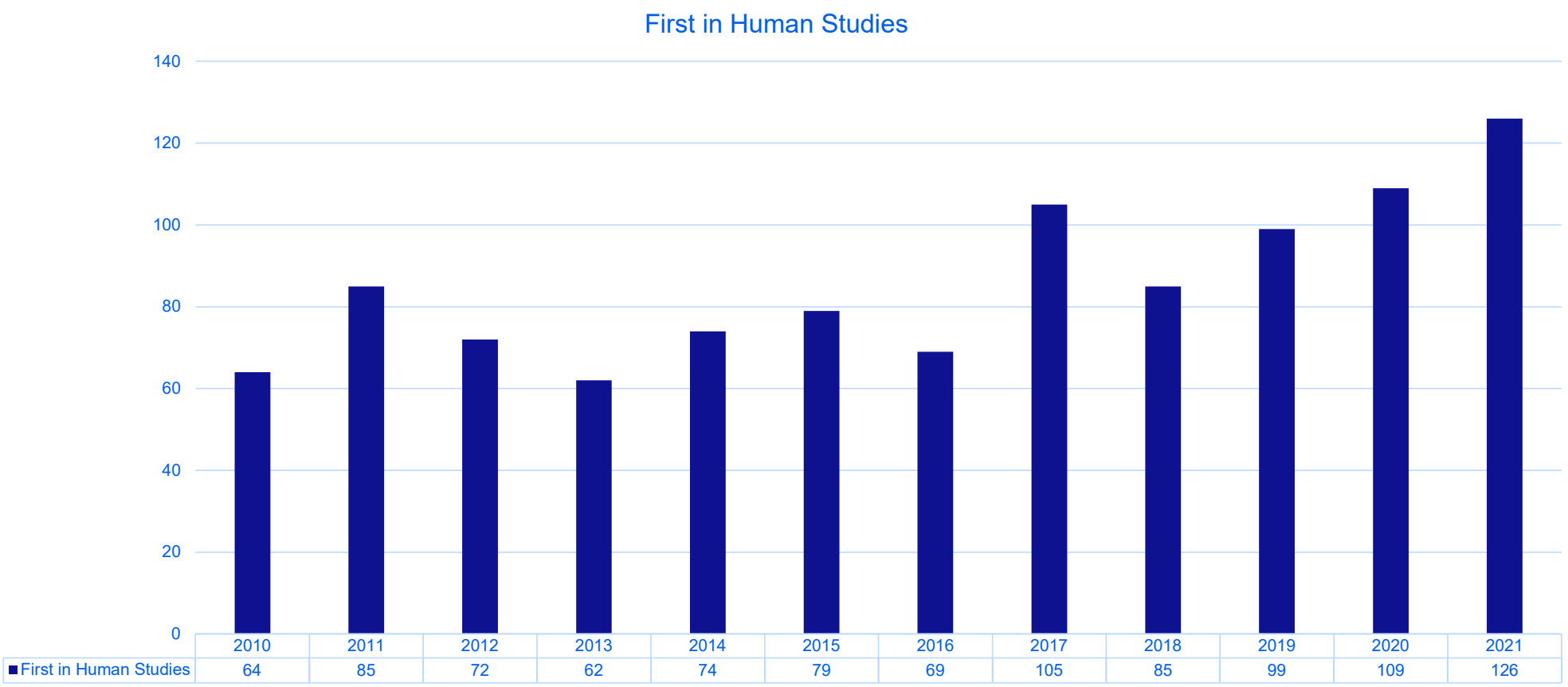



| Apr-21 | May-21 | Jun-21 | Jul-21 | Aug-21 | Sep-21 | Oct-21 | Nov-21 | Dec-21 | Jan-22 | Feb-22 | Mar-22 |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 22 | 17 | 18 | 22 | 26 | 34 | 29 | 41 | 38 | | | |
| 54 | 49 | 55 | 70 | 59 | 55 | 67 | 38 | 36 | | | |

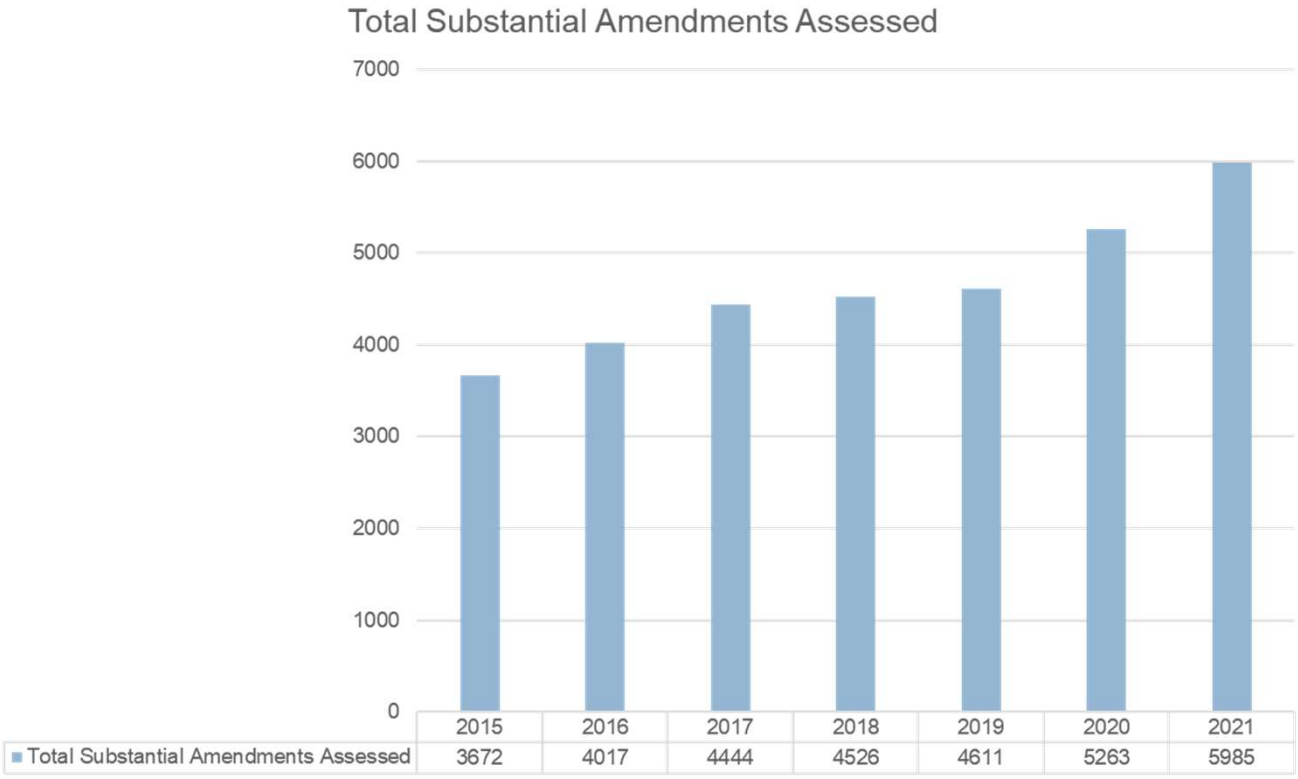


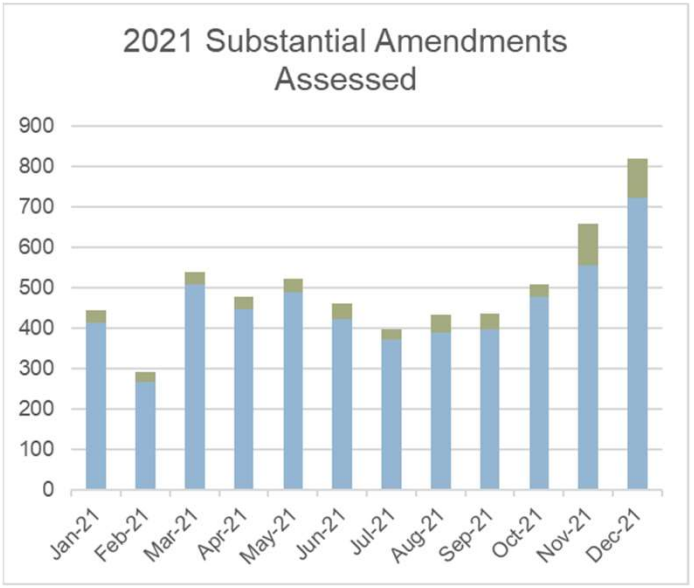

| | 2021 GNA | 2021 Approved |
|---|---|---|
| Average of 1st Review | 28.03 | 25.56 |
| Average of Time Awaiting GNA response | 17.97 | |
| Average of 2nd Review | 6.53 | |

# First in Human studies

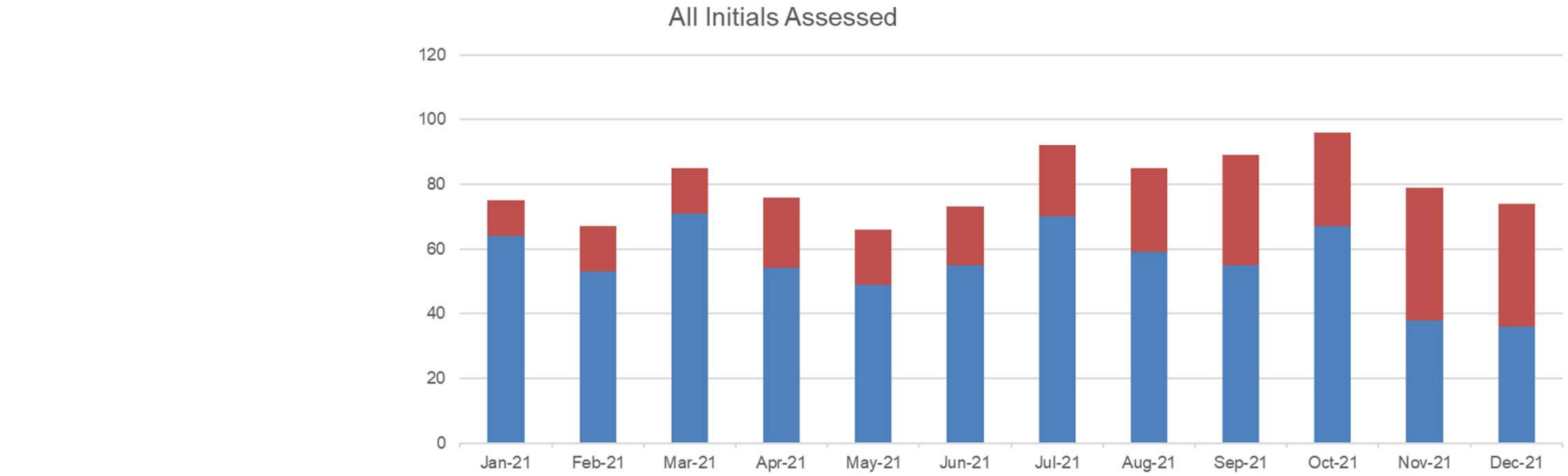


# Total amendments



# Combined review studies

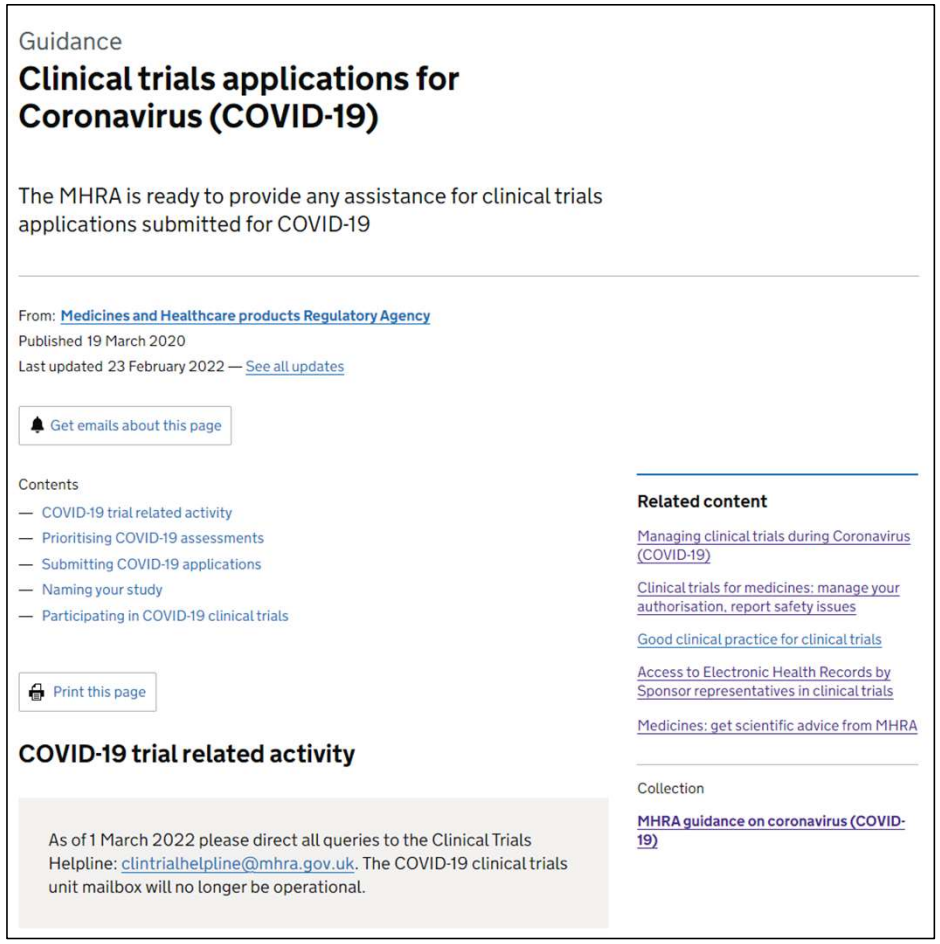



| | Jan-21 | Feb-21 | Mar-21 | Apr-21 | May-21 | Jun-21 | Jul-21 | Aug-21 | Sep-21 | Oct-21 | Nov-21 | Dec-21 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| CTAs Submitted through Combined Review Process | 11 | 14 | 14 | 22 | 17 | 18 | 22 | 26 | 34 | 29 | 41 | 38 |
| Standard CTAs | 64 | 53 | 71 | 54 | 49 | 55 | 70 | 59 | 55 | 67 | 38 | 36 |

# Combined review of CTIMPs

- On 1January, combined MHRA and research ethics committee review became the way all sponsors and applicants seek approval for new IMP Clinical Trials
- Combined review offers CTIMP applicants and sponsors a single application route (via new IRAS) and a joined-up review, leading to a single UK decision in a faster overall timeline than the previous separate processes
- Experience to date has shown that combined review can halve the time it takes for studies to get overall approval
- Note that trials submitted through combined review after 1 January will be automatically registered on the ISRCTN Registry when given full approval
- Further IRAS functionality for trials involving ionising radiation is to follow in 2022. The service will continue to be refined and developed in line with user feedback (including MHRA form).

# COVID trial applications



Guidance

**Clinical trials applications for Coronavirus (COVID-19)**

The MHRA is ready to provide any assistance for clinical trials applications submitted for COVID-19

From: Medicines and Healthcare products Regulatory Agency
Published 19 March 2020
Last updated 23 February 2022 — See all updates

Get emails about this page

Contents
- COVID-19 trial related activity
- Prioritising COVID-19 assessments
- Submitting COVID-19 applications
- Naming your study
- Participating in COVID-19 clinical trials

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**COVID-19 trial related activity**

As of 1 March 2022 please direct all queries to the Clinical Trials Helpline: clintrialhelpline@mhra.gov.uk. The COVID-19 clinical trials unit mailbox will no longer be operational.

**Related content**

Managing clinical trials during Coronavirus (COVID-19)

Clinical trials for medicines: manage your authorisation, report safety issues

Good clinical practice for clinical trials

Access to Electronic Health Records by Sponsor representatives in clinical trials

Medicines: get scientific advice from MHRA

Collection

MHRA guidance on coronavirus (COVID-19)

The clinical trials COVID-19 mailbox is no longer monitored

Covid.clinicaltrials@mhra.gov.uk

Please use the normal Helpline:

Clintrialhelpline@mhra.gov.uk

# Pilot of combined IMP/Device research

# Pilot of combined IMP/Device research

- Combined trials of an investigational medicinal product and an investigational medical device (IMP/Device trials) will also be submitted via the new combined review system, helping us take another step towards delivering the agency objective for a single decision on research using both a medicine and device
- We are calling on sponsors, research organisations and investigators running studies involving both a medicine (CT) and a medical device (CI) to join our CT/CI coordinated assessment pilot and contribute to develop a new streamlined route within the combined review journey.
- If you would like to express your interest in joining the pilot programme to benefit from the joint CT/CI assessment procedure, please email clintrialhelpline@mhra.gov.uk with the subject line “CT/CI Pilot”

# In Vitro Medical Devices (IVDs) pilot

- An IVD is used with “medical purpose” if it is used to determine eligibility and/or treatment assignment in a CT of a medicinal product: the output of the IVD has a significant impact on the safety of the trial participants and scientific value of the trial.

- We have developed risk-proportionate considerations for regulation of IVDs that should be addressed by Sponsors of trials incorporating an IVD with medical purpose and are working with a cohort of developers to refine these.

- If you want to contribute to shaping these requirements, please send an email to beatrice.panico@mhra.gov.uk subject line: IVD pilot.

- **Note: Under the new MHRA structure CT and CI teams sit within the same function in Science, Research and Innovation (SR&I)**

# Innovative licensing and Access Pathway

# Innovative Licensing and Access Pathway

- **Innovation Passport:** A new medicine designation links to the development of a roadmap to patient access
- **Target Development Profile** (TDP): Creates a unique UK roadmap, utilising tools from a toolkit and providing a platform for sustained multi-stakeholder collaboration
- **A toolkit**: tools are intended to drive efficiencies in the development programme, supporting data generation and evidence requirements
- **An integrated pathway**: Pulls together expertise from across the MHRA, NICE, SMC and AWTTC partners in the wider healthcare system including the NHS in England and Scotland, patient experts

# Tools being developed in the Toolkit

- Adaptive inspections
- Enhanced patient engagement
- Centre Accreditation
- UK HTA Access Forum
- Certifications
- New licensing procedures:
  - Rolling review
  - Accelerated timetables for marketing authorisation flexibilities
  - International options
- Continuous benefit-risk assessments that integrate real word evidence
- Novel CT methodology & design support
- CPRD control groups
- CPRD assisted recruitment in clinical trials
- Rapid Clinical Trial Dossier pre-assessment service
- Common medicine & device trial design
- Coordinated approvals process for co-developed medicines & IVDs

# ILAP IP activity 2021

- 76 applications (Oncology 25, neurology 13, respiratory 7), 44 granted, 23 pending, 8 refused, 1 withdrawn

- Variety of sized companies – large and small, spinout from UK university
- Includes products for FDA Orbis in oncology (11 IP applications expressed specific interest)
- Rare and common diseases

- First Innovation Passport
- Issued for treatment developed in a rare condition
  - von Hippel Lindau disease

Press release

**First Innovation Passport awarded to help support development and access to cutting-edge medicines**

The Innovative Licensing and Access Pathway (ILAP) aims to reduce the time to market for innovative medicines

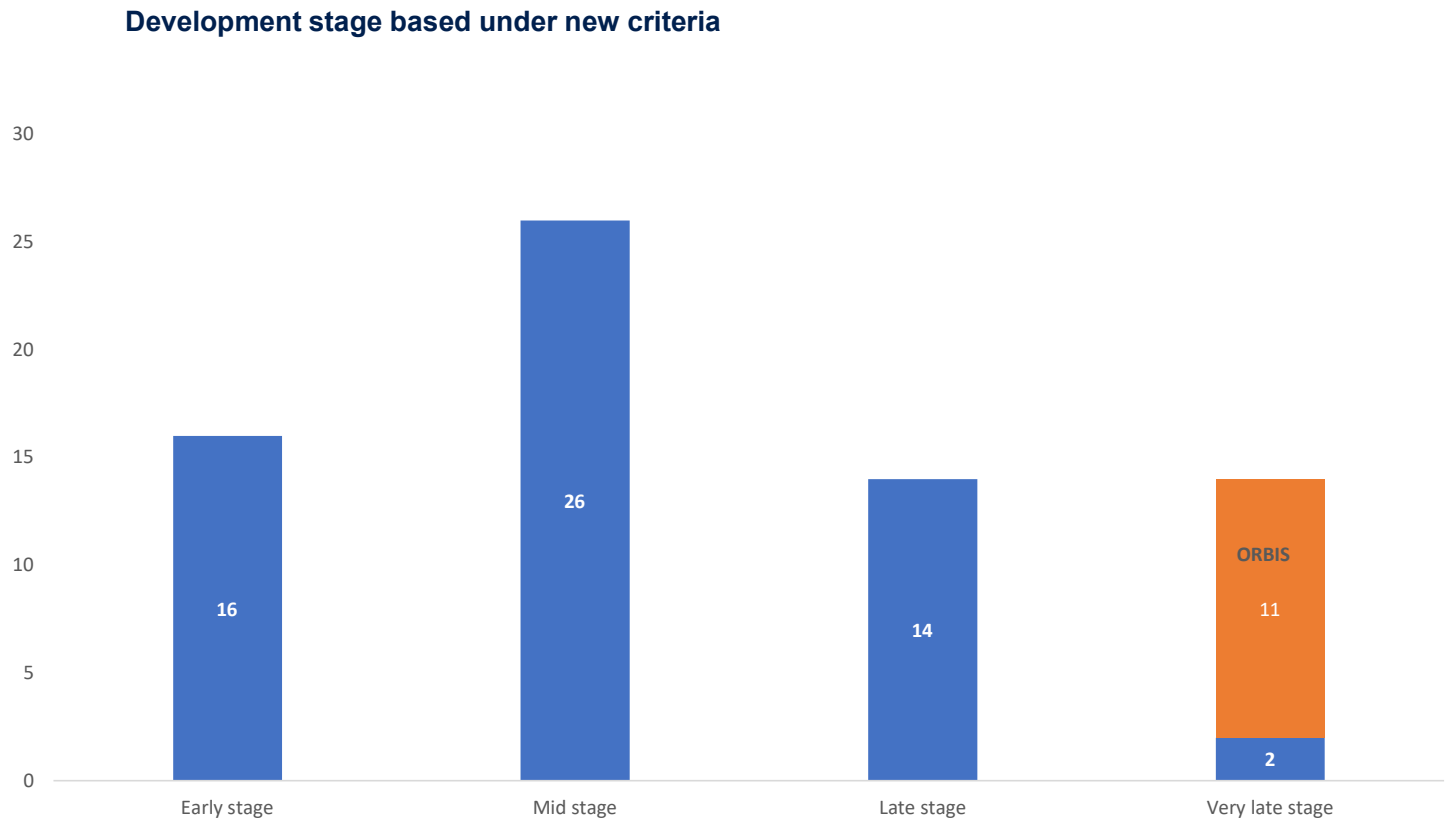
From: Medicines and Healthcare products Regulatory Agency
Published: 26 February 2021

MHRA

A promising treatment for a cancer-causing rare disease will be the first to pass a significant milestone under a new UK approval process designed to bring medicines more rapidly to patients.

Belzutifan, a treatment developed by MSD (UK) for adults with von Hippel Lindau disease (a rare genetic disorder that causes cancer) has been awarded the first 'Innovation Passport' by the Medicines and Healthcare products Regulatory Agency, National Institute for Health and Care Excellence and the Scottish Medicines Consortium (SMC).

# IP applications by development stage




**Early stage**:

First in human study not yet initiated, no clinical data available

**Mid Stage**

Phase 1 and or non-confirmatory phase 2 clinical trials ongoing or conducted, pre-phase 3 (not recruiting), early clinical data available on efficacy and safety

**Late Stage**

Confirmatory phase 2 or phase 3 trial on going or completed, significant clinical data available

**Very Late Stage**

Imminent Marketing Authorisation (MA) submission

# CTR update

https://www.ema.europa.eu/en/human-regulatory/research-development/clinical-trials/clinical-trials-regulation


- Clinical Trials Information System (CTIS) will go live on 31st January 2022
- There is a 3 year transition period – EudraCT will not be used for new CTA applications after January 2023

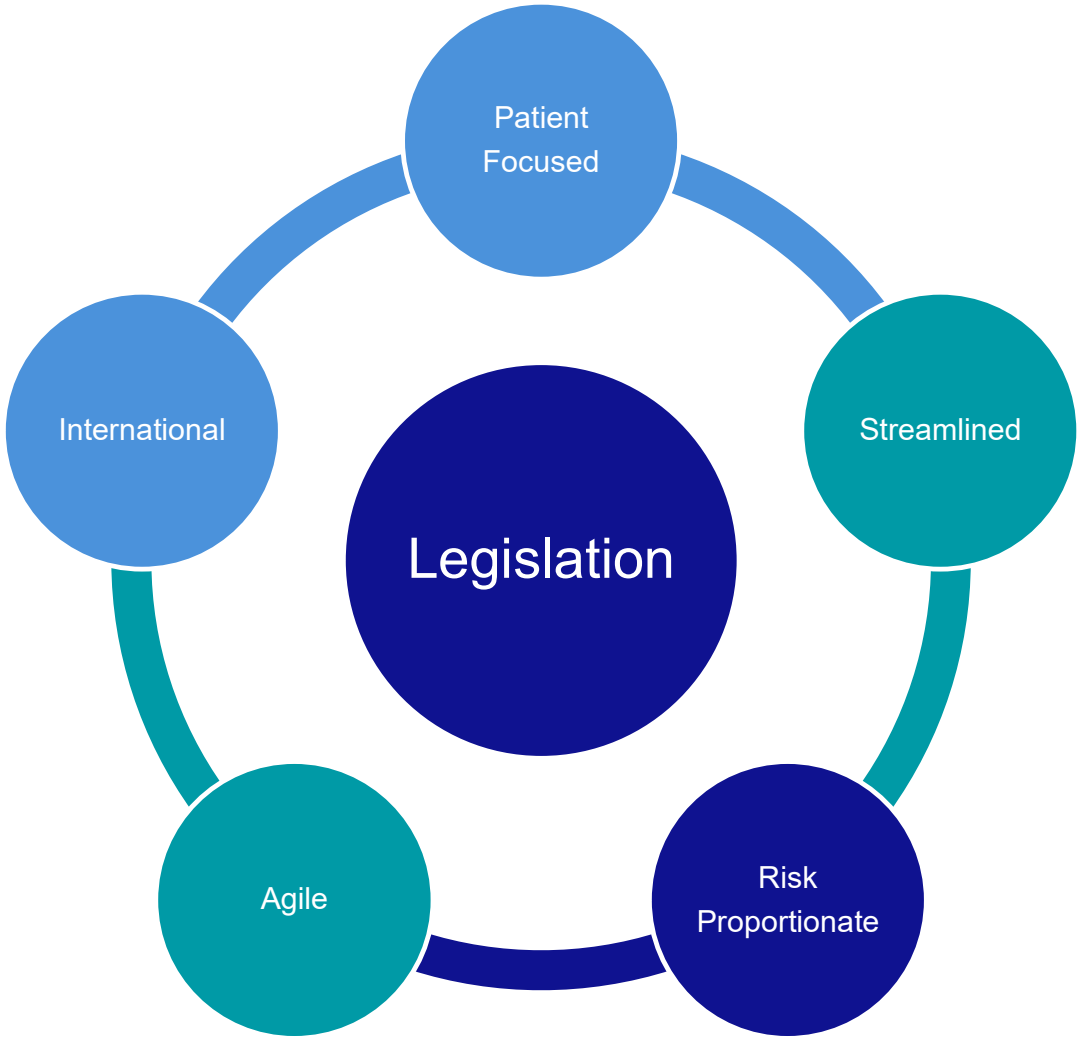
- There is extensive training and support online, as well as a modular training programme and many Q&A documents for each element of a new CTA and maintaining a CTA

- The CTR will not take effect in Northern Ireland – this remains under the remit of MHRA as part of ‘UK’ regulation
- Aware the addition of patient ‘rights’ in the serious breach definition may have caused some concern. EMA had a draft guideline in 2017 but this does not provide a specific example.
- Sponsors will need to consider updating their SOPs to account for the new CTR as well as UK legislation if conducting multinational trials.

- Any questions for MHRA – please direct to the CT Helpline: clintrialhelpline@mhra.gov.uk

# Legislation updates


Medicines & Healthcare products Regulatory Agency
Open consultation
Proposals for legislative changes for clinical trials
Published 17 January 2022
Medicines & Healthcare products Regulatory Agency
#ResearchSavesLives


Patient Focused
Streamlined
Risk Proportionate
Agile
International
Legislation

# Patient Focused

- Current UK legislation, based on the 2001 EU Directive, is silent on clinical trial transparency and patient involvement in trial design.
- Propose to legislate for some of the research transparency provisions policies and processes set out in the HRA ‘Make it Public’ strategy, to embed research transparency in the regulation of clinical trials.
- This also includes involvement of people with relevant lived experience in the design, management, conduct and dissemination of a trial.
- We are also exploring if legislative requirements support diversity in clinical trial populations.

# Streamlined

- Embed combined review' procedure into legislation
- Maintain UK competitive timelines for approval but provide flexibility for sponsors to respond to questions raised
- Remove duplicate reporting of Suspected Unexpected Serious Adverse Reaction (SUSARs) also allow these to be reported in an aggregate manner, where appropriate
- Remove requirement for line listing in annual safety reports - instead include an appropriate discussion of signals/risks associated with the use of the medicinal product as well as proposed mitigation actions.

# Risk Proportionate

- A key element of our proposals is empowering researchers to take more risk appropriate approaches to trial life cycle
- For trials where the risk is similar to that of standard medical care, we are proposing a “notification scheme” where the clinical trial can be approved without the need for a regulatory review and should be conducted in a risk-proportionate manner.
- Open question on principles of Good Clinical Practice (GCP) that we should put in legislation that reflect risk proportionality.
- Proposals to facilitate ‘cluster trials’ (eg randomisation by region)

# Agile

- We do not wish to extend the scope of the current legislation or add legislation where it is more appropriate and flexible to develop best practice guidance or promote pragmatic interpretation of the legislation.

- The consultation proposes removal of granular requirements in the current legislation to be replaced by guidance wherever possible.

- Guidance will be co-developed with relevant external experts and stakeholders, including patients and trial participants to ensure consistent and pragmatic interpretation of legislation and flexibility to respond rapidly to future innovation and progress.

# International

- A key aim is to ensure our legislation enhances our attractiveness for international partnerships so that the UK remains a preferred site to conduct multi-national trials.
- Proposals maintain international standards for trial conduct whilst introducing streamlined, efficient and competitive approvals for trials.
- Definitions updated to promote international harmonisation where trials have sites across Europe.

- The consultation closed on March 14th and all the responses are now being reviewed.
- A Government response to the comments will be published in due course.
- MHRA will also be drafting the new guidance and legal teams will be drafting the new legislative wording

# Questions?

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