MHRA experience with CIDs and recommendations derived from it

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MHRA continues to support novel trials

CTFG paper link

Nature / BJC paper link

Clinical Trial Transformation Initiative (CTTI)

https://www.ctti-clinicaltrials.org/projects/master-protocol-studies

- Regulators (FDA, MHRA), academia, industry, consultants developed a guide to Master Protocol trials
- Set of tools to guide appropriate use of master protocols
- Launched: 13th of October 2020
- Pre-planning tools, as well as planning and implementation, study simulation tool and protocol development map

MHRA implementation plan for novel trials as part of LSIS

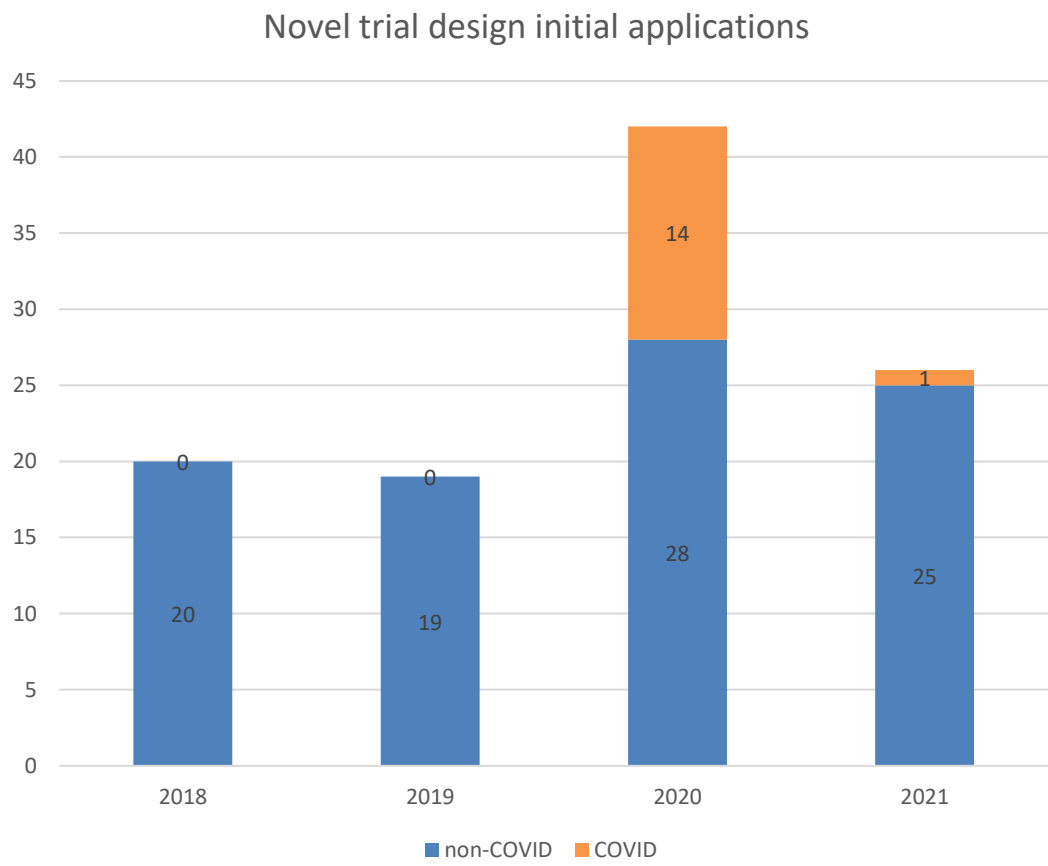
- Key outcome: Strengthened UK environment for clinical research that provides support for innovative trial design
- Included
  - Engagement with stakeholders on novel trials and our advice services
  - Workshop – October 2020
  - Internal training
  - Report

Metrics – inc. novel trial designs in COVID-19

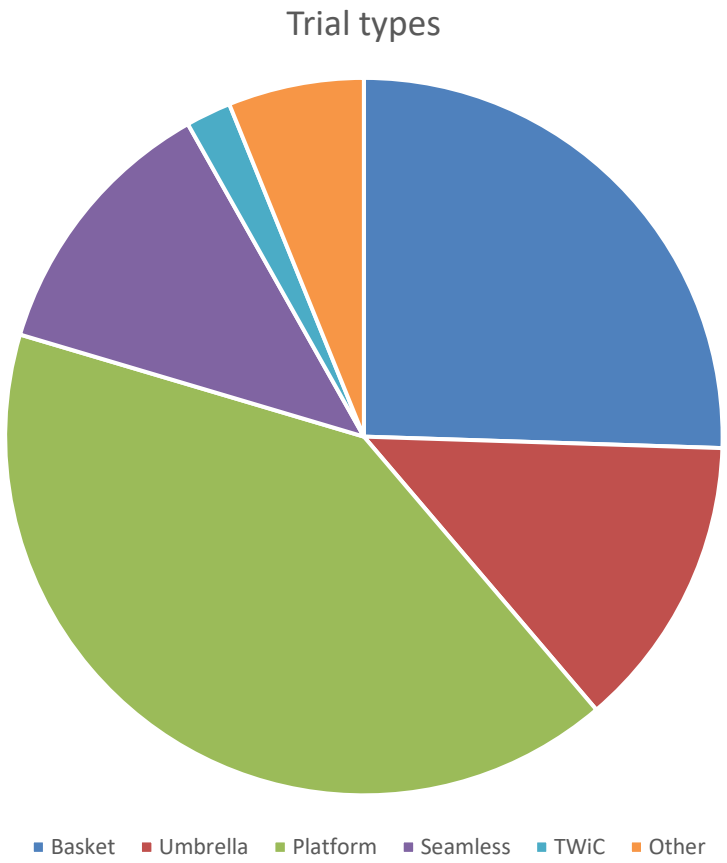
MHRA CTU has been tracking these trials since January 2018.

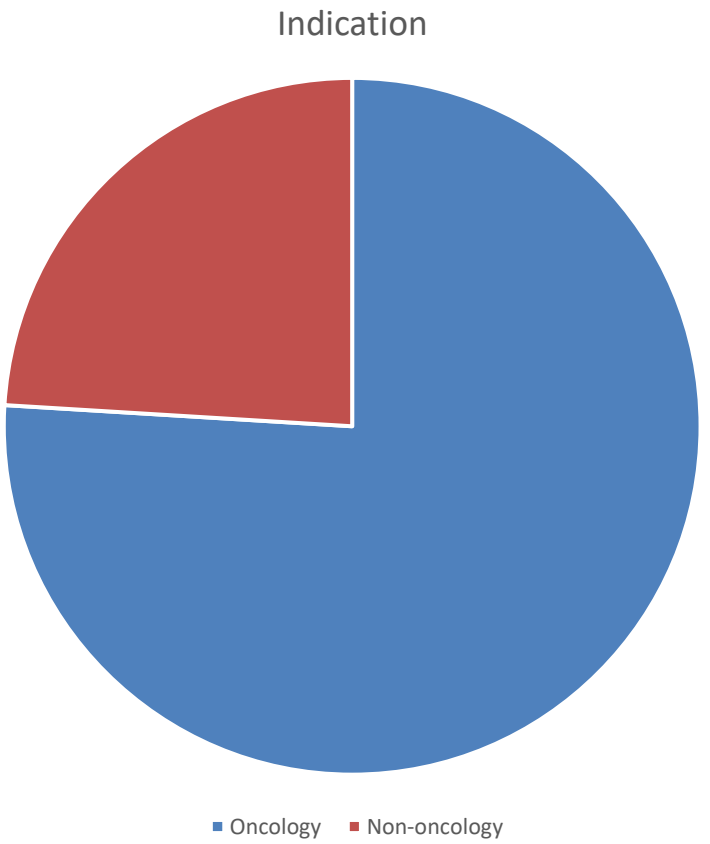
COVID-19 saw a rise in submissions – supported by NIHR and Chief Medical Officer

- Recovery
- Principle
- REMAP-CAP
- Others…..



Metrics


Trial types
Basket
Umbrella
Platform
Seamless
TWiC
Other


Indication
Oncology
Non-oncology

Recommendations

The biggest barrier to innovation and research from our perspective is not coming to ask our advice early enough (or at all !)

- Scientific advice
- Broader scope meetings
- Regulatory advice
- Innovation office meetings

Novel trial designs must, like all trials, be safe and scientifically sound. Specific guidance is available, but it is just that – guidance. It is not included in legislative requirements. Each trial is reviewed on a case-by-case basis.

Key elements to consider – CTFG recommendation paper

Recommendation	Further consideration
Clearly describe and justify the design	Some national competent authorities (NCAs) (not the MHRA) do not accept that First-in-human IMPs and Advanced Therapy Medicinal Products (ATMPs) are introduced via substantial amendments; some NCAs (not the MHRA) do not support trials with several independent arms and prefer they are submitted as separate trials.
Maintain scientific integrity	The scientific hypothesis and primary objectives defined at the time of the initial CTA application should not be changed during the conduct of the trial.
Ensure quality of trial conduct and optimise clinical feasibility	Investigator and Sponsor oversight
Ensure safety of trial subjects	Independent Data Monitoring Committee (IDMC), communication plan
Maintain data integrity	Type 1 error rate, confidentiality of interim results versus transparency
Reassess benefit-risk balance at critical steps	Throughout a clinical trial: in case of safety signals, at the time of substantial amendments, consider changes of informed consent form (ICF)
Validate companion diagnostics	In vitro diagnostic medical devices (IVDs)
Consider data transparency	publication policy, some NCAs require submission of data within one year (six months for paediatric trials) following the end of a sub-protocol (not absolute requirement for MHRA)

Innovative Licensing and Access Pathway

- **Goal**: to deliver efficient and timely development of medicines and earlier patient access

- A new medicine designation links to the development of a roadmap to patient access – **Innovation Passport**

- **Target Development Profile** (TDP) creates a unique UK roadmap, utilising tools from a toolkit and providing a platform for sustained mutli-stakeholder collaboration

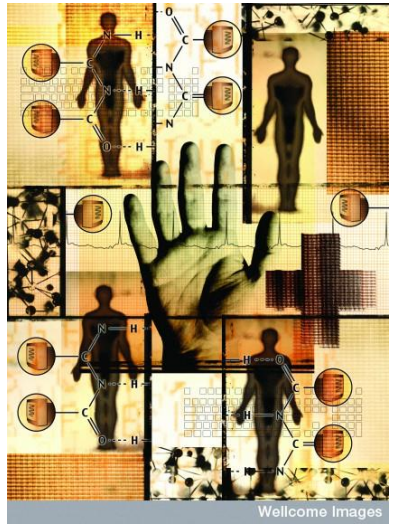
- The regulatory toolkit is intended to drive efficiencies in the development programme, supporting data generation and evidence requirements

- An integrated pathway will pull together expertise from across the MHRA and partners in the wider healthcare system including NICE and the SMC

- Built-in flexibility, with multiple entry points along the pathway (non-clinical data → clinical trials)

Some of the tools being developed in the Toolkit

- Adaptive inspections
- ATMP Centre accreditation*
- Novel CT methodology & design support
- Common medicine & device trial design
- Coordinated approvals process for co-developed medicines & IVDs
- CPRD assisted recruitment in clinical trials
- Rapid Clinical Trial Dossier pre-assessment service
- Certifications



- CPRD control groups
- Enhanced patient engagement
- Continuous benefit-risk assessments that integrate real word evidence
- New licensing procedures:
  - Rolling review
  - Accelerated timetables for marketing authorisation, flexibilities
  - International options
    - FDA Orbis
    - ACCESS

*contact GCP.inspectorate@mhra.gov.uk

Summary

Integrated approach to support innovation in design through continued engagement with industry, charities, patients and research bodies such as the ECMC.

Develop components of a regulatory toolkit composed of required components (tools that ensure regulatory compliance) as well as those that can be selected individually to support a bespoke development programme that reflects a lifecycle approach to evidence generation.

Questions?

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