

**End-to-end performance metrics: 2016-2017**

This report consists of metrics obtained by combining data from:

* the Medicines and Healthcare Products Regulatory Agency (MHRA) on date of submission for clinical trial authorisation and date of authorisation, for clinical trials of investigational medicinal products only
* the NIHR reports on performance of initiation and delivery of research, on date of first participant recruited to study and on date of first NHS decision of capacity and capability (and date of first recruit at that site) for all types of clinical trials
* HRA on date of IRAS submission and date of HRA Approval

Data relating to MHRA submissions relates to clinical trials of investigational medicinal products (CTIMPs) only. Data on ‘all clinical trials’ relates to the first four categories of study type as set out in the IRAS application, ie CTIMPs, clinical investigations of devices, trials of combined medicinal products and devices, and other clinical trials. Note that the majority of the commercial studies reported are CTIMPs, whereas the majority of the non-commercial studies are other types of clinical trials.

The data reported relates to submissions made from March 2016 with a data cut-off at collection of data of May 2018. A distinction is drawn between studies submitted up to August 2017 and those submitted up to April 2018. The data relating to submissions from March 2016-August 2017 consisted of a fairly consistent number of applications per month and is therefore deemed to be representative of the sample of studies that had recruited within a year from submission.

Of the CTIMPs submitted during this period to July 2017, 74% of the commercial clinical trials had recruited a first participant and were included in the data, whereas 65% of the non-commercial clinical trials had recruited a first participant. It is important to note, therefore, that the data presented do not include timelines for studies that failed to recruit within one year of the first regulatory submission.

For data presented through to April 2018, the sample of studies per month decreased from August 2017 as an increasing number had not yet recruited by May 2018 due to the shorter time available. This report does not, therefore, give a full picture across all trials, but is biased towards the better performing studies. Data to April 2018 is further biased to the best performing studies, with the intention of demonstrating what is possible. However, trends over time during the period from March 2016 to August 2017 reflect a consistent number of studies and are therefore believed to reflect real changes in performance rather than being an artefact of a biased sample.

No account is taken in this report of the complexity of the study, whether the participants were from a rare disease, or the reason for lack of progression.

**1. Median timelines in calendar days based on the month of application submission to MHRA or IRAS to the first patient recruited, showing the period of submission from March 2016-July 2017**

* Red line shows median time from MHRA submission to first participant recruited to study
* Purple line shows median time from IRAS submission to first participant recruited to study for clinical trials of investigational medicinal products only
* Blue line shows median time from IRAS submission to first participant recruited to study for all types of clinical trials

This shows an overall decrease in time from both MHRA and IRAS submission to first participant for clinical trials of medicines (CTIMPs) with a fairly level timeline for other types of trials. This decrease is less pronounced than seen previously for applications up to April 2017, reflecting the impact of the slowest recruiting studies where time to recruitment was greater than one year.

**2. Median timelines in calendar days based on the month of application submission to MHRA or IRAS to the first patient recruited, showing the period of submission from March 2016 to April 2018**

**Sample of better performing studies**

* Red line shows median time from MHRA submission to first participant recruited to study
* Purple line shows median time from IRAS submission to first participant recruited to study for clinical trials of investigational medicinal products only
* Blue line shows median time from IRAS submission to first participant recruited to study for all types of clinical trials

Figure 2 continues through to April 2018 (last available data), although the number of studies represented decreases significantly over time from August 2017, as fewer and fewer studies had recruited a first participant at the cut-off date. The data over this later period therefore shows the median time for the sample of better performing studies.

The data from submissions in 2018, although biased to the sample that had recruited within the available time, shows that it is possible for efficient clinical trials to be set up in around 100 days from first regulatory application to first participant recruited.

**3. Median timelines in calendar days based on the month of application submission to MHRA or IRAS from March 2016-April2018 (commercial) and Jan 2018 (non-commercial) to the first patient recruited**

* Red line shows median time from MHRA submission to first participant recruited to study
* Purple line shows median time from IRAS submission to first participant recruited to study for clinical trials of investigational medicinal products only
* Blue line shows median time from IRAS submission to first participant recruited to study for all types of clinical trials

Figure 3 splits the data by commercially and non-commercially sponsored study types, showing that overall the timelines for commercial studies are more predictable and the overall data is skewed by more outliers in the non-commercial studies. Non-commercial data is shown up to January as there were no studies submitted beyond that date that had recruited at the point the data was cut. The commercial data also shows a more consistent downward trend with clear demonstration of the potential delivery times for better performing studies.

**4. MHRA Submissions (medians) to first recruit in study, showing timelines from individual stages of the process to first recruit**

This graph shows the time taken from each stage of the approval process through to first recruitment. This demonstrates the time taken for the various stages. The data starts from MHRA submission and does not include the separate IRAS submission, which is usually after MHRA submission. The purpose is to show the breakdown of the end-to-end timelines from first regulatory submission.

* Blue bar shows median time from MHRA submission to first participant recruited
* Red bar shows median time from MHRA clinical trial authorisation to first participant recruited
* Green bar shows median time from HRA Approval to first participant recruited
* Purple bar shows median time from NHS decision of capacity and capability at first site to first participant recruited (not necessarily at that site)

Figure 4 shows that the timeline from NHS decision to first participant recruited has not changed much, whereas the time from preceding steps to first participant has reduced.

Figure 5 explores this further by examining the time for individual stages of the overall set-up process.

**5. MHRA Submissions (medians) to first recruit in study, showing timelines of each individual stage of the process**

* Blue section shows median time from MHRA submission to MHRA authorisation
* Red section shows median time from MHRA authorisation to HRA Approval
* Green section shows median time from HRA Approval to NHS decision of capacity and capability
* Purple section shows median time from NHS decision of capacity and capability at first site to first participant recruited

Figure 5 shows that there has been little change in the time from NHS decision at first site to recruitment of the first participant (not necessarily at the same site). Similarly the time from MHRA submission to MHRA authorisation has remained relatively static. An improvement in time from MHRA authorisation to HRA Approval took place during 2016 reflecting improvement in the HRA Approval timelines and greater parallel processing of applications through HRA and MHRA. However there has been less improvement in the timelines for site set-up and recruitment.

**Summary**

This data shows that some clinical trials are completing the end-to-end process from first regulatory submission to first participant recruited within 100 days, with some completing in even less time. Further analysis of the features of these efficient studies is needed. However, anecdotal feedback suggests that the following tend to be seen in commercial studies that complete the approval process faster:

* Parallel submission of the IRAS form and MHRA form
* High quality submissions with all required documents included first time (frequently missing documents for commercial studies include the validated costing template and the contract), allowing initial assessment to proceed promptly
* Ensuring that the participant information sheet follows HRA guidance, thus avoiding a provisional opinion from the REC
* Parallel invitation to sites while the approval process is underway (possible when the correct documents are submitted so initial assessment can proceed)
* Agreeing target timelines for set-up and recruitment with sites

These factors will be increasingly important as the MHRA and the UK research ethics service continue to pilot a combined way of working consisting of a single submission and integrated review process.