Advice for Management of Clinical trials in relation to Coronavirus

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MHRA are aware that there are challenges arising in relation to Coronavirus and the effect this is having on the conduct of clinical trials. Patients may be advised to stay away from hospitals and GP sites due to existing health problems that may put them at risk of infection, or they may be reluctant to travel to sites where there are high densities of people. They may also have been advised to self-isolate as a precaution or as a result of confirmed infection so are unable to undertake required clinical trial activities. Organisations managing and sponsoring clinical trials are also experiencing a higher proportion of staff working from home during this period.

This has led to reports of protocol and standard operating procedure deviations due to missed visits, or changes in processes, for example posting out drug to patients. Wet-ink signatures have also been difficult to obtain in a timely manner if staff are not in the office, and this can delay some clinical trial processes.

We recognise the difficulties this creates for managing trials and would like to offer some advice.

There will be an increase in protocol deviations; please ensure they are well documented, to enable appropriate evaluation for the trial.

An increase in protocol deviations in relation to Coronavirus will not constitute a serious breach, therefore there is no need to report this to us (unless of course patients are being put at risk).

Resources may need to be assessed in hospital settings, with staff working primarily in research being required to assist in other areas. This may mean certain oversight duties, such as monitoring and quality assurance activities might need to be reassessed and alternative proportionate mechanisms of oversight introduced (such as phone calls, video calls etc) to ensure ongoing subject safety and well-being. We would advise a brief risk assessment and documentation of the impact of this, with consideration of prioritisation of critical activities such as safety reporting. Remote monitoring can be considered; however, this should not place an extra burden on trial sites, and subjects must consent to any sharing of their personal information outside the trial site.

Prospective protocol waivers remain unacceptable, we would not expect you to bypass the eligibility process due to difficulties in assessing subjects and carrying out tests. Safety of

patients of course remains a priority and they should not be included into a trial unless you can confirm they meet the inclusion and exclusion criteria. Similarly, if the safety of a trial subject is at risk because they cannot complete key evaluations or adhere to critical mitigation steps, then consideration to discontinuing that subject must be discussed. This may also extend to the whole trial in some cases, and a Sponsor and Investigator should not forget they are able to use Urgent Safety Measures, or even temporarily halt a trial, or halt recruitment, if this is the best way forward. Do note that we are requesting that any temporary halt, including for logistical reasons such as trial team unavailability, should be submitted as a substantial amendment (which will be fast-tracked). This is to ensure MHRA has complete oversight of status and safety for these trials.

Subject safety is of course our highest priority, Sponsors should consider the risk/benefit of conducting trials in medicines that act as immunosuppressants, for example in early phase healthy volunteer trials, where there is no therapeutic benefit to the volunteer, but taking part in the trials does pose a risk of infection.

If your processes require wet-ink signatures, consider alternative methods of demonstrating approvals, such as email confirmation. Inspectors will take a pragmatic approach to this, but you may want to consider an SOP deviation to cover this in the interim.