**Summary overview of the Clinical Trials Regulation (EU) 536/2014**

**Implications and opportunities for PREPARE and pandemic clinical research**

**What is the Clinical Trials Regulation (EU) 536/2014?**

The Clinical Trials Regulation (EU) 536/2014 is legislation governing the regulation of all clinical trials of medicines conducted in Europe. It does not apply to non-interventional studies. The Regulation was approved by the European Parliament on 16 April 2014 and is expected to come into effect by October 2018. The Regulation replaces the Clinical Trials Directive 2001/20/EC and will be legally binding in all EU member states. The Regulation aims at harmonisation of practice across EU member states, thereby making it easier to conduct multi-site, multi-country clinical trials.

There is currently no provision in the Regulation for clinical trials being conducted during a public health emergency that might arise from an infectious disease outbreak or bioterrorist incident. There is opportunity to influence a change when the Regulation is reviewed (every 5 years).

**Implications and opportunities for pandemic clinical research**

While there are many unknowns about how the Regulation will be fully implemented in EU member states, some features may offer opportunities for PREPARE in developing outbreak response plans.

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| **Features of the Regulation** | **Opportunities for pandemic research** | **Considerations for PREPARE**  |
| A single application dossier for a clinical trial is submitted through the EU portal for assessment in two parts. The first part is subject to a coordinated review by all concerned member states with one member state that will act as the “reporting member state” taking the lead. The second part is subject to review by each relevant member state and deals with national issues (e.g. informed consent, site suitability).  | No need for duplicate submissions that meet unique requirements of different EU member states. This represents an opportunity for PREPARE in reducing the time to prepare and obtain approval for new multi-country clinical trials.  | * Develop an application pro-forma that includes as much pre-populated information as possible.
* Plan to submit application dossier parts 1 and 2 together.
* Identify clinical sites in EU member states that have expedited review processes. Note: clinical trial can start once a member state has had part 2 approved.
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| Review timeframes are binding across all members states:* 45 days for initial assessment (additional 31 days may be added if questions need to be asked).
 | Establishes greater predictability for researchers. Reduces variability across member states. However, expedited review processes in each member state not mandated, therefore variability for expedited review still anticipated.  | * Ensure part 1 of the application dossier is submitted to an EU member state that has expedited review.
* Engage regulatory authorities in EU member states where expedited mechanisms do not exist during inter-pandemic periods to consider how these mechanisms might be established – opportunity to do this now as EU member states start to consider how to re-organise themselves in preparation for the Regulation to take effect.
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| New category of clinical study: “low intervention study” that is subject to “less stringent rules” compared with other clinical studies – i.e. a proportionate, risk-based approach. | Makes it easier to do studies evaluating routinely used medications, such as comparative effectiveness studies. Also easier to do some paediatric studies, e.g. evaluations of medications routinely used off-label where evidence-based and supported by published scientific evidence.  | * Engage regulatory authorities in EU member states to consider acceptability of alternate informed consent procedures for low intervention studies – e.g. for PREPARE in outbreak response mode.
* Consider and justify classification where current PREPARE studies and sleeping protocols might be considered low intervention.
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| Co-sponsorship  | Potential for public-private partnerships |  |