Table 1: EARL barriers and potential solutions

| BARRIER | TOWARD A SOLUTION |
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| **Funding**- Barriers related to access to funding and flexibility of contracts  | **1.** Rapid access to prioritized research funding (GloPID-R)**2.** Prioritisation of funding specifically for pandemic studies (e.g. NIHR HTA) **3.** Lobbying for funding **4.** A rapidly prioritised research agenda by expert panel to focus the scientific response and identify priorities for funding. **5.** Contracts that allow flexible and rapid movement of funds between European project partner Institutions for pandemic research response.  |
| **Protocol development**- Time delay related to study planning, protocol development and development of study materials | **1.** Pre-identification of research question, study methods, standardised case definitions, participant information, consent forms in pre-approved, “sleeping “ protocols. A well-developed study maintenance plan to ensure readiness. 2. Pre-approval of protocols included in international guidelines for pandemic clinical research preparedness**3..** Universally agreed case definitions, pre-approved protocols, case report forms, data collection forms, adverse event reporting (ISARIC). 4. Set-up of studies during inter-pandemic peacetime. 5. Use of novel trial designs e.g. platform trials, adaptive design  |
| **Ethical and regulatory approvals** - Time delays- Lack of harmonisation | **1.** Fast-track ethical/regulatory approvals specific to emerging outbreaks/epidemics/pandemics**2.** Pre-approvals**3.** Regulatory changes **4.** Set-up of specific ethics boards, develop close relationship and training of ethics boards/regulators (e.g. novel trial design, pandemic research) |
| **Contracting and Sponsorship*** Time delays; Variable practice across countries, regions and institutions; Varied perception of risk
 | **1.** Pre-approved contracts (at least agreement of generic phrases across Institutions and countries)**2.** Closer liaison with Sponsor/Contracts teams and provision of training (e.g. risk of research, research scenarios)**3.** Agreement that is accepted by all countries and ‘one shop’ approval for all member states |
| **Recruitment of study sites and recruiters** | **1.** Development of research networks, e.g. GRACE, PREPARE**2.** Local mentors (experienced recruiters to act as local research champions to engage other sites)**3.** Identification of issues that are impeding pandemic research in specific areas (e.g. paediatric research) |
| **Research ready research network and trained staff**- Pandemic research response requires established research networks and trained staff with capacity to conduct research in pandemic | **1.** Established PREPARE research networks across Europe (primary, secondary and tertiary care, participant specific (e.g. children) **2.** Dedicated research task force with adequate research capacity to conduct research in pandemic**3.** Preparation of training materials and rapid, focused training mechanisms**4.** Tracking of trained staff, identification of replacement staff (where necessary) and regular updating of training |
| **Relationship with Public Health agencies**- Research effort must be aligned to first line national/ global public health response teams  | **1.** Established working relationships with Public Health/Health Protection/Emergency Response teams who respond to pandemics |
| **Participant identification**-In some cases e.g. influenza, the public have had messages to ‘stay away from primary care’ and self-care, so may not present to clinical recruiting site unless very sick or too late in clinical course for medication impact (antivirals in first 3 days); Clinical trials costly - ideally only those patients with a confirmed condition would be recruited. But clinical symptoms are non-specific and identifying patients who have the condition of interest challenging.  | **1.** Learning lessons from PREPARE studies (innovative participant identification) **2.** Involvement of professional groups in addition to teams in clinical setting (e.g. pharmacy staff)**3.** Local ‘public engagement’ campaigns (various media)**4.** Optimising information provision to potential participants with sign-posting to recruitment site (e.g. cascade through public health information channels, families, influenza clinics, pharmacies)**5.** Development of specific and sensitive diagnostic tests for the identification of new and emerging diseases (especially viral diseases).**6.** Development of universally agreed case definitions (special panel that can be rapidly convened). |
| **Participant recruitment**-Participant recruitment is one of the major obstacles to successful studies- Recruitment poses a significant barrier in relation to time and capacity of recruiting clinicians.- Recruitment of participants considered a ‘vulnerable population’ – e.g. paediatrics or pregnant women in studies: recruiters may be nervous of recruiting- Capturing all potential patients to increase internal and external validity | **1.** Design of research studies that answer/consider questions that are perceived as important by members of the public (potential participants) and clinicians (potential recruiters).**2.** Design of research procedures (e.g. alternative consent) that are acceptable to all key stakeholders: ethics boards, potential participants, clinicians, researchers, (and potentially public health bodies). **3.** Identification of ways to expedite research (e.g. alternative enrolment procedures, recruitment by non-clinicians e.g. trained medical students or other health professionals like pharmacists). **4.** Design research that considers/implements community engagement strategies**5.** Design of studies that minimise the number of participants that are needed to recruit for successful outcome (adaptive, platform trials).6. Embedding clinical research into clinical practice |
| **Access to routine clinical samples and data for research**- Consent not normally in place to use (anonymised) routine clinical data, excess clinical samples (blood, swabs) or samples collected for surveillance/public health measures- Excess clinical samples not routinely stored (lack of Biobanking facilities) or not stored in consistent and optimal ways -There can be legal and technical (country specific) problems with export of data  | **1.** Implement and promote collection of biological samples and data for research in clinical settings.**2.** Putting in place an acceptable and feasible consent process that can be used within clinical care process and is acceptable to all stakeholders (Research consent as part of clinical consent)**3.** Pre-approved research materials (posters, patient information and consent forms (ideally should cover DNA research – genetic markers of risk groups and personalised medicine).**4.** Pre-approved protocols to enable collection of standardised data; and collection and storage of samples **5.** Training of clinical staff **6.** Engagement with public health/clinical process decision makers**7.** Developing Biobanking facilities and processes |
| **Preparedness of Laboratories**Lack of diagnostics capability (staffing, equipment and relevant training), lack of standardized protocols, inadequate tests and sample accessibility | **1.** Engagement of laboratories and assessment of capability and requirements **2.** Pre-approved standardized protocols for collection, storing and sharing of samples and data**3.** Staff training**4.** Logistics (sample transport and sharing – necessary for diagnostics and potentially vaccine development) |
| **New vaccines /medications (IMP) in trials**-Potential logistical hurdles may be encountered in production of new vaccines/medication (can take 6 months and many steps with country specific differences); Availability of IMP for research and IMP storage for research may be issue in pandemic.  | **1.** Learn lessons from seasonal influenza vaccine delivery and implement clear procedures for pandemic research requiring vaccines**2.** Understand how supplies are tracked and track supply chains to avoid running out**3.** Consider alternatives and substitutions. |
| **Capability of systems to pivot to response mode in the event of a pandemic**- Relevant to ‘peacetime’ studies and ‘sleeping protocols’ - can be resource intensive; should be planned and tested.  | **1.** Design and implementation of platform/adaptive trials**2.** Regular contingency planning and testing (peacetime trials and sleeping protocols)**3.** Ensure communications with outbreak committees (e.g. WHO and Public health Response teams)**4.** Consider location of trials: High incidence/outbreak risk settings |