ESF Science Meeting, Brussels, Belgium, 12-13 December 2012

PREPARE Meeting 2012

Scientific report

1) Summary

TRACE (partners) are involved in the project proposal PREPARE (Platform foR European Preparedness Against (Re-)emerging Epidemics) invited to submit a full proposal for Stage 2 in response to the 7th Framework Programme Call Innovative health research 2013 of the European Commission HEALTH.2013.2.3.3-1. Clinical management of patients in severe epidemics. FP7-HEALTH-2013-INNOVATION-1.

Currently, there is no coherent framework for the rapid implementation of cross-border harmonised clinical research studies in the event of an emerging epidemic. However, such studies are needed to provide clinical evidence in support of optimal patient management. At present, the field essentially needs to start from scratch during each new epidemic in recruiting sites, developing protocols, obtaining ethical and regulatory approvals, training clinicians and recruiting patients. Moreover, established networks that do manage to implement clinical trials at the earliest stages of an epidemic are typically restricted to regional or national levels, not covering the required breadth and size of patient groups necessary to draw useful clinical conclusions. The PREPARE project has been designed to address the bottlenecks of implementing timely clinical research in response to emerging epidemics. It establishes a network of networks, that combines common procedures and systems and "on the shelf" validated and pre-approved protocols with a clear governance structure to initiate immediately large scale pan-European clinical research studies addressing key clinical questions in the event of an emerging epidemic.

PREPARE will achieve this by 1) overcoming current ethical and regulatory hurdles for rapid approval of clinical research, 2) consolidating a pan-European network and infrastructure that supports coordinated international clinical collaboration and data exchange, 3) designing a new clinical research practice that is tuned to the nature of epidemics, and allows rapid large-scale internationally harmonised research, 4) developing supportive SOPs that are internationally recognised and 5) training network staff to implement these SOPs when needed. The inter-pandemic research programme will result in the following valuable output: 1) insights into current impact, etiologies and management of relevant infectious disease (ID) syndromes in Europe, 2) evidence-based guidance documents for the clinical management of ID, 3) pathophysiological insights to guide development of personalised clinical management strategies of ID, 4) whole genome mapping and sequencing outbreak tools, and 5) innovative point-of-care diagnostics.

In the new state-of-the-art evidence-based arena, international clinical trials of meaningful statistical power can start days after an outbreak has been detected and in clinically-relevant time span produce the insights needed to assess public health risks, to diagnose and stratify patient groups, to select optimal treatments and treatment regimens and importantly to effectively distribute this knowledge in and beyond European healthcare organisations. In addition, the insights and developments generated during intra- and inter- pandemic periods allow the development of novel preventive and therapeutic personalised clinical management

strategies relevant for current clinical practice and potential future outbreaks. Thus far, no organisation or network in Europe has been able to build the infrastructure required for this endeavour. PREPARE will lay the foundations for a new paradigm in clinical management of patients in ID pandemics thereby reducing the public health-and economic damage.

In this PREPARE meeting scientists affiliated with institutions funding TRACE and other institutions discussed the evaluation of the PREPARE Stage 1 proposal. Furthermore a concept of the different work packages for the Stage 2 proposal was presented, focusing on the pathogenesis work packages and those on clinical trials. This conference resulted in a work plan and timing to develop a successful proposal for Stage 2.

Description of the scientific content of and discussions at the event

The background of the FP7 call was presented by Jeremy Farrar, highlighting that an infectious disease outbreak usually last only 6 weeks and that it will be a major challenge to bring the 611 days average between idea and the inclusion of the first patient down to the ideal of 3 days between outbreak and the inclusion of the first patient. Herman Goossens introduced PREPARE. He focussed on the text of call and the evaluation of the Stage 1 proposal. Next he presented the conceptual structure of PREPARE. It was questioned whether or not to add research in children, but it was felt that no exceptions could be made for children given the existence of other vulnerable group, e.g. the elderly and immunocompromised.

Next the Core network and consortia were presented, including the EU funded projects, ANTIGONE and EMPERIE by Ab Osterhaus, PREDEMICS by Sylvie van der Werf, and RAPP-ID by Herman Goossens. Chris Butler presented GRACE and its ESF funded successor TRACE as the primary care network, Herman Goossens COMBACTE as the envisaged hospital network, and Mike Sharland the paediatric network PENTA-ID. Again the importance of looking at children was discussed.

The work package descriptions and discussions started with Alistair Nichol (WP1). It was concluded that the EC should be the one pulling the trigger for initiation of PREPARE's pandemic response, since the EC funds PREPARE. Frank Leus presented WP2 on the online database. It was concluded that the analysis of the data would be part of the WP3 clinical studies. Caroline Brown presented the education and training work package (WP6). There was strong advice to focus on the clinical centres with these activities, since this is specifically asked in the call.

After a short intermezzo on FP7 essentials, the work packages on pathogenesis and on the clinical trials were discussed in detail during two breakout sessions in parallel.
Regarding the clinical trials (WP3) it was decided to split this into several separate work packages. Once again it was discussed whether or not research in children should be dealt with in a separate work package. For each of the different WPs leads for the writing process were assigned, and others invited to join their team.
For the pathogenesis work package (WP4) a similar strategy was adopted. In addition, it was concluded that in concordance with the WP3 study that would deliver the WP4 samples that data is collected for different age populations and various infections.

On day 2 of the meeting it was agreed to focus the discussion on the work package(s) on clinical trials. It was decided to use the qualitative methods described by Chris Butler in WP1 and WP6. Marion Koopmans explained how the suggested observational study would be different from surveillance. Theo Verheij reviewed the proposed design, intervention and outcome of the intervention study. It was decided to integrate the best available test at the time of the study. A concise presentation of the adaptive trial design was given by Jeremy Farrar. Within the ISARIC network there is ample expertise to support this work package.

The meeting concluded with a wrap up of the tasks for each of the PREPARE partners to ensure that a strong and successful Stage 2 proposal will be submitted by February 6, 2013.

Assessment of the results and impact of the event on the future directions of the field

Most importantly, an events like this, supported by the European Science Foundation through TRACE, has the potential to impact substantially on the development of new translational research on antimicrobial resistance and community acquired infections in Europe and beyond. The meeting greatly increased the chances of delivering a successful Stage 2 proposal in response to the 7th Framework Programme Call Innovative health research 2013 of the European Commission HEALTH.2013.2.3.3-1. Clinical management of patients in severe epidemics. FP7-HEALTH-2013-INNOVATION-1. If successful, PREPARE aims to establish a pan-European clinical research network and infrastructure for immediate 'on-demand' implementation of harmonised, large-scale clinical research studies in the context of emerging infectious outbreaks with pandemic or epidemic potential and provide the necessary evidence base for an optimal clinical management response.

Annexes: programme of the meeting and full list of speakers and participants.

Annex I

Meeting programme

PREPARE Meeting 2012, Brussels, Belgium, 12-13 December 2012

Agenda PREPARE Meeting

Day 1

08.30 - 08.40 Opening and welcome (Herman Goossens)*

08.40 - 09.00 Introduction of all participants

09.00 - 09.30 Background of the FP7 call (Jeremy Farrar)*

09.30 - 10.15 Introduction PREPARE (Herman Goossens)*

- Meeting objectives and deliverables
- Meeting agenda
- Call tekst
- Stage-1 proposal and evaluation (strengths and weaknesses)
- PREPARE conceptual structure
- WPs and Participant task division

10.15 - 10.30 Discussion

10.30 - 11.00 Coffee / tea break

11.00 - 12.30 Presentation of Core networks and consortia
Menno de Jong*: ANTIGONE and EMPERIE
Sylvie van der Werf: PREDEMICS
Herman Goossens*: RAPP-ID
Chris Butler*: GRACE
Marc Bonten*: COMBACTE (*Herman Goossens*)
Jean-Daniel Chiche: ICU
Mike Sharland: Peadiatric network

12.30 - 13.30 lunch break

13.30 - 14.30 WP1 (Alistair Nichol)

14.30 - 15.00 WP2 (Frank Leus)*

15.00 - 15.30 Coffee / tea break

15.30 - 16.30 WP6 (Caroline Brown)

16.30 - 17.00 FP7 crash course incl. essentials, clinical trials, budget rules (Frank Deege, Jochem Bossenbroek)

17.00 - 19.00 Breakout sessions:
1. Clinical trials
2. Pathogenesis

20.00 Dinner at Brussels Sheraton Airport Hotel

Day 2

08.30 - 09.30 Adaptive trial design, WP3.5 (Jeremy Farrar)*

09.30 - 10.30 Trials WP3.1 en 3.4 (Chris Butler)*

10.30 - 11.00 Trials WP3.3 (Marion Koopmans)

11.00 - 11.30 Coffee / tea break

11.30 - 12.00 Trials WP3.2 and WP 4 (Menno de Jong)*

12.00 - 12.30 WP5 (Greet Ieven)*

12.30 - 13.30 Lunch break

13.30 - 15.00 Governance and decision making processes (Herman Goossens)*
- Project governance
- Interpandemic Clinical trial governance
- Pandemic Clinical response
- Interaction with PREPARE Networks, Consortia and Boards

15.00 - 16.00 Wrap up
- TTOPSTART
- Question round
- AOM
- Conclusions
- Take home message

* scientists affiliated with institutions funding TRACE

Annex II

List of speakers and participants*

Title	Full name	Gender	Affiliation, comprising full professional address Email address
Prof	Samuel Coenen	Male	University of Antwerp, Centre for General Practice and Laboratory of Medical Microbiology, Vaccine & Infectious Disease Institute (VAXINFECTIO), Universiteitsplein 1, 2610 Antwerp, Belgium
Prof	Theo JM Verheij	Male	Julius Center for Health Sciences and Primary Care, UMC Utrecht, PO Box 85500, 3508 GA Utrecht, The Netherlands
Prof	Chris C Butler	Male	Cardiff University, Institute of Primary Care and Public Health, 5th Floor, Neuadd Meirionnydd, Heath Park, Cardiff CF14 4XN, United Kingdom
	Charles Auffray	Male	Université de Lyon 50, avenue Tony Garnier 69007 Lyon, France
	Marc Bonten	Male	UMC Utrecht Heidelberglaan 100 3584 CX Utrecht
Mr	Jochem Bossenbroeck	Male	Ttopstart Staalweg 30 3721 TJ Bilthoven The Netherlands
Dr	Caroline Brown	Female	WHO Scherfigsvej 8 2100 Copenhagen Denmark
	Gail Carson	Female	University of Oxford, ISARIC Churchill Hospital Oxford OX3 7LE UK
Ms	Tanja Cermaes	Female	Ttopstart Staalweg 30 3721 TJ Bilthoven The Netherlands
	Menno De Jong	Male	AMC Departement of Medical Microbiology Meibergdreef 9 1105 AZ Amsterdam The Netherlands
	Frank Deege	Male	Erasmus MC 's Gravendijkwal 230 3015 CE Rotterdam The Netherlands
	Jeremy Farrar	Male	190 Benham Tu Quan 5 Hochi Minh Vietnam

	Pieter Fraaij	Male	Erasmus 's gravendijkwal, dept urology 3015 CE Rotterdam The Netherlands
Prof	Herman Goossens	Male	Universiteit Antwerpen, Medical microbiology Universiteitsplein 1 2610 Wilrijk Belgium
Prof	Greet Ieven	Female	UZA Wilrijkstraat 10 2650 Edegem Belgium
	Marion Koopmans	Female	RIVM Antonie van Leeuwenhoeklaan 9 3720 BA Bilthoven The Netherlands
	Frank Leus	Male	UMC Utrecht Heidelberglaan 100 3584CX Utrecht The Netherlands
Dr	Dieter Maier	Male	Biomax Robert Koch strasse 2 82152 Planegg Germany
Prof	Surbhi Malhotra	Female	Universiteit Antwerpen, Medical microbiology Universiteitsplein 1 2610 Wilrijk Belgium
	David Nauwelaers	Male	Biocartis Generaal De Wittelaan 24 2800 Mechelen Belgium
	Alistair Nichol	Male	UCD, School of Medical Science Belfield Dublin 4 Ireland
Ms	Sophie Nys	Female	Universiteit Antwerpen, Medical microbiology Universiteitsplein 1 2610 Wilrijk Belgium
Prof	Peter Openshaw	male	National Heart & Lung Institute Imperial College London Norfolk Place, St Mary's campus, Paddington, London, UK
Prof	Ab Osterhaus	Male	Erasmus MC Dr Molewaterplein 50 3000 CARotterdam Nederland
	Matthias Pletz	Male	Jena University Hospital Erlanjer Allee 101 07740 Jena Germany
	Mike Sharland	Male	St George University London Pediatric Infectious Diseases Blackhorse Road

			SW70 QT UK
Dr	Federico Torres	Male	Universitario de Santiago de Compostela Traversia da Choupana 15706 Santiago de Compostela Espana
Mr	Carlos Triay	Male	Arttic 58 A, rue du Dessous des Berges 75013 Paris France
Prof	Alex van Belkum		Biomeriux 3 Route de Port Michaud 38390 La Balme les Grottes France
	Sylvie van der Werf	Female	Institut Pasteur Unité de Génétique Moléculaire des virus à ARN 28 Rue Dr Roux 75724 Paris, France
	Jorge Villacian	male	Janssen Diagnostics 2340 Beerse Belgium
	Geert Maertens	male	Biocartis Generaal de Wittelaan 11 B3 2800 mechelen Belgium
	Jean-Daniel Chiche	male	Hôpital de Cochin Paris Rue du Faubourg St jacques 75014 Paris, France