REPORT

Workshop towards the Coordination of Publicly Funded Clinical Studies and Trials on Infectious Diseases during Outbreaks

14 - 15 May 2024

The ARC
SQUARE – Brussels
Convention Center Mont des Arts/Kunstberg
Brussels, Belgium

Foreword

Pandemics require a rapid and coordinated response and the COVID-19 pandemic has demonstrated that the EU is a crucial actor when dealing with health crises. This pandemic brought a major shock to health systems of EU Member States and exposed weaknesses in our collective defences against health threats. For instance, during the pandemic, an unprecedented number of academic clinical trials had been launched by the Member States. Despite these efforts, **a lack of coordination across Member States** resulted in a chaotic landscape with numerous underpowered trials that could not provide meaningful results and a duplication of research activities. Yet, clinical trials are the cornerstone of the generation of reliable evidence on safety and effectiveness of interventions against infectious diseases during pandemics.

The failure of a rapid, coordinated clinical research response in the EU can be explained by many reasons that caused **fragmentation of EU clinical research**: no coordination of funding and too many small unimpactful national trials were funded by the Member States; no prioritisation of clinical research; no coordination between the different clinical trial networks; and no top-down political support to participate in large scale EU-funded clinical trials. Arguably today, the EU is not better prepared for a rapid clinical research response to a new pandemic threat than it was when the COVID-19 pandemic started. In fact, fragmentation **has worsened** with the COVID-19 pandemic due to a plethora of (often not coordinated) activities and initiatives.

The **Belgian Presidency of the Council of the EU** during the first half of 2024 focused on three major themes: “care”, “preparedness” and “security”. Under the slogan “a Europe that cares, prepares and protects”, we organised a workshop on 14 and 15 May 2024 “towards Coordination of Publicly Funded Clinical Studies and Trials on Infectious Diseases during Outbreaks”. In this context, the Belgian EU Presidency aimed to expand the EU’s capacity to conduct large scale clinical trials.

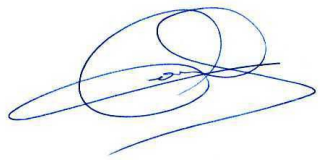
We started preparing this workshop during the summer of 2023. The **first step** was to build a comprehensive database of public and charity funding resources of clinical studies and trials for infectious disease in Europe. The **second step** was to conduct a survey with the aims: (i) to understand funders’ experiences in supporting clinical studies in Europe before and during the pandemic; (ii) to understand funding policies and selection processes and; (iii) to compare public funding allocated before and during the pandemic. The **third step** was to conduct qualitative interviews of funding organisations that participated in the survey. The aim of these interviews was to gain insights into the challenges and obstacles faced at the national level to fund clinical research and to collect more in-depth information relevant to establishing an efficient coordination mechanism for multi-country clinical studies and trials on infectious diseases. During **the workshop on 14 and 15 May 2024**, the preliminary results of the survey and interviews were presented, alongside case studies from national funders. A full report with the final results will be available by the end of 2024.

This **report summarises the presentations and discussions during the workshop**. After the welcoming speech of Frank Vandenbroucke, Belgian Deputy Prime Minister and Minister of Health and Social Affairs, the potential threats of future pandemics, the lessons learned of the clinical research response during the COVID-19 pandemic, the activities of the Health Emergency

Preparedness and Response (HERA) and other EU initiatives, the warm-based laboratory networks, and the Clinical Trial Networks were discussed. Subsequently, the future European Partnership for Pandemic Preparedness was discussed, and the preliminary results of the survey and interviews were presented. Four case studies of national funding of clinical research were presented, followed by a general discussion on future coordination of funding. The workshop programme and presentations can be consulted on the website of the University of Antwerp at this link.

This **Belgian EU Presidency workshop was unique in many ways**. For the first time, a comprehensive database of national funders of clinical research was built. For the first time, these national funders met and shared their experiences. For the first time, all the Clinical Trial Networks met and shared their plans. Therefore, we hope that this workshop will serve as a foundation for exploring a mechanism to coordinate public funding of clinical research during pandemics.

In conclusion, **the COVID-19 pandemic is a wake-up call** and there will be no better time and opportunity than now to overcome the fragmentation of health research in Europe. Without significant and sustained efforts to build stronger collaboration between the Member States and EC services, the EU will fail and stand accused of having turned its back on the prospect of tackling pandemic infectious diseases, to the detriment of the health and wellbeing of its citizens.



Em. Prof. Dr. Herman Goossens
University of Antwerp
Belgium
Coordinator of the EU Presidency Workshop

Acknowledgement

Establishing a coordinated approach for public funding during future infectious disease outbreaks is an effort undertaken by many committed individual experts and stakeholders. However, we would like to take this opportunity to extend our special thanks to Frank Vandenbroucke, Belgian Deputy Prime Minister and Minister of Health and Social Affairs, for his tireless and visionary dedication to public health and for delivering a thought-provoking opening speech. We also extend our gratitude to Dirk Ramaekers, Chair of the Federal Public Service Health, Food Chain Safety and Environment, and Gloria Ghéquière, Adviser Belgian Council Presidency, for their support and enthusiasm.

We thank the speakers for their inspiring presentations and for fuelling the workshop discussions:

- Christian Drosten
- Cornelius Schmaltz
- Surbhi Malhotra-Kumar
- Evelina Tacconelli
- Maya Hites
- Inge Christoffer Olsen
- Carlo Giaquinto
- Oliver Cornely
- Victoria C. Simensen
- Laurent Jaboeuf
- Safia Thaminy
- Frank Hulstaert
- Arne Flåøyen
- Kate Gerrand
- Mike Rogers
- Ralf Heyder

We express gratitude to all participants for their valuable and active contributions to the workshop.

Finally, the workshop would not have been possible without the constructive inputs from the many colleagues of the ECRAID-Base, BE READY and VACCELERATE consortia, throughout the preparation and development of the event.

The workshop was organized in the framework of the Belgian Presidency of the Council of the EU and funded through the European Union's Horizon 2020 ECRAID-Base project and the Belgian Federal Office for Health, Food Chain Safety and Environment.

Contents

Opening speech by Frank Vandenbroucke, Belgian Deputy Prime Minister and Minister of Health and Social Affairs

Belgian Health Minister Frank Vandenbroucke begins by outlining the policy priorities of the Belgian Presidency of the European Council, which he characterizes with three themes: "a Europe that cares, prepares, and protects." The minister emphasizes the need for Europe to address health workforce shortages, prioritize unmet health needs, and enhance crisis preparedness. He highlights efforts to manage medicine shortages and reduce dependencies on pharmaceutical supplies, including the establishment of a voluntary solidarity mechanism among Member States and a critical medicines alliance aimed at creating a robust framework for addressing these issues.

Minister Vandenbroucke reflects on the dual challenges of antimicrobial resistance (AMR) and lessons from the COVID-19 pandemic. He recounts Belgium's historical actions against AMR, noting the impact of EU cooperation in reducing antibiotic prescriptions and fostering collaborative efforts. Despite achievements, he stresses the importance of continued momentum to prevent and control antimicrobial resistance. On COVID-19, he acknowledges initial failures in solidarity and preparedness among EU Member States and calls for improved coordination and response planning. He highlights Belgium's proactive steps, including an assessment by the European Centre for Disease Prevention and Control (ECDC) on their national outbreak response planning.

Addressing the need for better coordination in clinical trials during health crises, the minister points out the confusion caused by underpowered and uncoordinated trials during the COVID-19 pandemic. He advocates for a European ecosystem for public clinical trial platforms to ensure rapid, high-quality research outputs in future pandemics. He expresses optimism that the workshop will inspire concrete actions to strengthen this ecosystem and emphasizes the inevitability of future pandemics, urging preparedness. At the same time, he acknowledges the fact that the road towards a common mechanism for better coordination of funding during future pandemics may be a long and winding one.

Minister Vandenbroucke concludes by underlining the importance of a consistent and ambitious EU health agenda, calling for the necessary resources to achieve this. He trusts that the Belgian 2024 Presidency will be seen as a pivotal moment in advancing the EU's preparedness and response to health crises.

Will there be a new pandemic and what are the potential threats?

Christian Drosten - Charité Berlin, Germany

In this lecture, Prof. Christian Drosten discusses the mechanisms and principles behind potential future pandemics. He begins by acknowledging the uncertainty inherent in predicting the next pandemic, but he stresses the importance of understanding principles and mechanisms of infectious diseases. The speaker cites the Spanish flu and COVID-19 as paramount examples of pandemics caused by respiratory pathogens, which are primarily transmitted through the air. Respiratory pathogens are of particular concern due to their ease of transmission.

Prof. Drosten then turns to vector-borne diseases, which often affect the tropical zone but are gradually making their way to Europe. He mentions Zika and Chikungunya as examples of diseases that are nearly pandemic in scope within the tropical zone.

One of the primary candidates for the next pandemic, according to Prof. Drosten, is Influenza A, particularly the H5N1 serotype. He explains the concept of "mixing vessels," where swine farms facilitate the transmission of viruses from birds to mammals. Recent observations suggest that direct transmission from birds to mammals, including humans, is also occurring. This underscores the importance of the One Health approach, which integrates human, animal, and environmental health.

Prof. Drosten highlights the global spread of H5N1, describing it as a pan-zoonotic virus with a 50% fatality rate in humans, although this figure likely reflects under-ascertainment. He notes that while human-to-human transmission of H5N1 is rare, recent increases in mammalian outbreaks, especially among feral carnivores and commercial fur farms, are concerning. He details an outbreak among housecats in Poland linked to commercial meat, illustrating the complexity of virus transmission.

A particularly alarming development is the detection of H5N1 in cattle in the U.S., where about 20% of milk samples tested positive for the virus. Prof. Drosten emphasizes that although the virus is not yet highly infectious to humans, its presence in the milk supply is concerning, and the transmission mechanisms among cattle are not well understood.

Prof. Drosten also discusses Middle East Respiratory Syndrome (MERS), a zoonotic disease primarily affecting the Arabian Peninsula. He outlines the virus's transmission from camels to humans, leading to nosocomial outbreaks in hospitals. Despite its limited human-to-human transmission, the virus's evolution and potential for increased transmissibility remain a concern. He notes that several vaccines are in clinical development, but more work is needed to ensure preparedness.

West Nile Virus (WNV) is another example Prof. Drosten uses to highlight the potential for localized outbreaks rather than global pandemics. He describes WNV's transmission cycle involving songbirds and Culex mosquitoes, which are common in Europe. The virus causes severe neurological disease in a small percentage of cases, predominantly affecting the elderly and immunosuppressed. Prof. Drosten discusses the challenges in developing a human vaccine for WNV, given the sporadic nature of outbreaks and the difficulty in conducting efficacy trials.

To conclude, Prof. Drosten emphasizes the need for robust surveillance systems and clinical study networks to detect and respond to emerging infectious diseases. He underscores the importance of preparedness, particularly for respiratory pathogens like Influenza A, zoonotic diseases like MERS, and vector-borne diseases like WNV. The speaker calls for continued vigilance and research to mitigate the impact of future pandemics.

Clinical research response during the COVID-19 pandemic: Lessons learned and how to prepare for the next pandemic

Herman Goossens - University of Antwerp, Belgium

Prof. Herman Goossens provides an overview of the development and history of clinical trial networks, emphasizing the importance of understanding this background for national funders and remote participants of the workshop. Clinical trial networks began to take shape in 1991 with the establishment of the global paediatric Research Network, primarily focused on HIV in paediatric infectious diseases. This initiative was led by Prof. Carlo Giaquinto, who later founded the PENTA Foundation in 2004 to address various paediatric infectious diseases beyond HIV.

In 2006, the next step in building clinical trial networks was taken through the GRACE program, which aimed to combat antibiotic resistance and community-acquired lower respiratory tract infections in Europe. This network was primarily sustained through successive project funding, a risky and unsustainable model.

By 2016, Prof. Goossens proposed a new model based on the Australian clinical trial network concept, which led to the creation of the European Clinical Research Alliance for Infectious Diseases (ECRAID). This model aims to create a unified network per disease or discipline to avoid competition and ensure harmonized activities. However, the landscape of clinical trial networks became more complex with the advent of the COVID-19 pandemic in 2020, which necessitated rapid adaptation and led to the creation of several new networks such as EU-RESPONSE and VACCELERATE.

Despite these advancements, Prof. Goossens points out the fragmentation and lack of strategic alignment among these networks, which became evident during the COVID-19 pandemic.

Lessons Learned from COVID-19

Key lessons learned from the COVID-19 pandemic based on work done in the PREPARE and RECOVER projects:

- Established structures and procedures: The most successful international trials, like REMAP-CAP and RECOVERY, have pre-established structures and procedures that facilitate rapid large-scale responses.
- Flexible and rapid EU funding: The EU funding for clinical research during COVID-19 was highly flexible and rapidly available, but lacked coordination between Member States and consensus on research priorities.
- Political and institutional support: There was insufficient political support and no top-down prioritization for EU-funded clinical studies. National studies often competed with European-wide studies, leading to fragmented efforts and redundant research.
- Inefficient use of resources: Clinical research infrastructures were not optimally utilized, and research was not sufficiently embedded into clinical practice.
- Administrative hurdles: Protocol and contract agreements took too long, and there was a significant variation in approval times for study protocols across EU countries.

Prof. Goossens highlights the differences between the REMAP-CAP and RECOVERY trials. REMAP-CAP, initially a European platform trial, struggled to gain participation and faced competition from national studies. Conversely, the RECOVERY trial benefited from an embedded research infrastructure within the UK's National Health Service (NHS) and urgent public health research status, which facilitated rapid inclusion and high participation rates.

The speaker also emphasizes the importance of the European Union presidencies as a tool for building a stronger European ecosystem for public clinical trials. He notes that engaging national funders in a cohesive strategy is essential for effective pandemic preparedness.

Recommendations for future pandemics

- Establishing an authority to oversee pandemic preparation and clinical research prioritization. The newly established HERA (Health Emergency Preparedness and Response Authority) addresses this need.
- An Outbreak Funding Mechanism (OFM) should be in place to rapidly leverage EU and national funding for pandemic response.
- Increasing investment in clinical trial networks, platform trials, and master protocols.

Conclusion

Prof. Goossens concludes by acknowledging that despite some improvements, the current state of fragmentation in clinical trial networks could potentially lead to an even less effective response in future pandemics. He calls for a sense of urgency in addressing these issues and stresses the need for dedicated leadership, political commitment, and strategic alignment between EU Member States and the European Commission to enhance pandemic preparedness.

Clinical Trial Coordination Mechanism for better health crisis preparedness and response

Cornelius Schmaltz, HERA, European Commission

In his talk, Dr. Cornelius Schmaltz focuses on the development of a new coordination mechanism for clinical trials aimed at enhancing health crisis preparedness and response within the EU. This initiative emerged from a workshop held last year, which brought together Member States and scientists in Amsterdam, organized by EMA, to review lessons learned from the COVID-19 pandemic. Key findings identified significant gaps, such as limited transparency regarding public funding sources, a lack of coordination in prioritizing promising products, and insufficient warm-based clinical trial networks, resulting in underpowered studies. These issues underscored the urgent need for a more cohesive EU-wide strategy to manage clinical trials and funding effectively during public health emergencies.

In response to these challenges, the Commission, alongside EMA, developed a proposal for a subgroup within the HERA Board. This subgroup is tasked with advising on the prioritization of clinical trials and their funding both in preparedness phases and during public health emergencies. Dr. Schmaltz outlines that the subgroup's work in preparedness would involve identifying and prioritizing product profiles and investigational medicinal products targeting high-priority threats, including pathogens with pandemic potential, antimicrobial resistance, and CBRN threats. It will also focus on developing a landscape of warm-based trials and strategic cohorts across the EU, ensuring coverage for vaccines and therapeutics. In a health emergency, the subgroup will provide expert opinions on identifying and prioritizing medicinal products based on EMA's scientific assessments and advise on suitable clinical trial networks and funding options to align EU and national resources.

The governance structure of this mechanism will see the HERA subgroup co-chaired by DG RTD and HERA, with HERA providing secretarial services. Dr. Schmaltz emphasizes the importance of a balanced composition, inviting Member States to nominate representatives with expertise in medicinal products, health, and research authorities. Additionally, permanent observers from EMA, ECDC, and HADEA, along with other relevant agencies, will participate in discussions. The subgroup will rely on two work streams: a dedicated group on identification and prioritization and the pandemic preparedness partnership, which will consolidate evidence-based input with a view to specific clinical research needs and the identification of the most suitable clinical trials sites to be developed both during preparedness and a public health crisis. This structure aims to enhance coordination and ensure the subgroup's recommendations are well-founded and actionable.

Dr. Schmaltz highlights the necessity of collaboration with existing clinical trial networks, academia, and industry stakeholders, acknowledging that the subgroup's success hinges on the collective effort and support of these groups. The proposal also addresses the EU's various funding mechanisms, such as Horizon Europe, EU4Health, and the Emergency Support Instrument, as well as national funding, which will support clinical trial networks, infrastructure, and multinational preparedness trials. For the future, Dr. Schmaltz mentions the upcoming nomination process for the subgroup, with a kick-off meeting slated for the end of June and the establishment of the working group for prioritization in July or August 2024.

Regarding the UK's involvement in the subgroup's prioritization, Dr. Schmaltz explains that while the subgroup's decisions will be heavily informed by the pandemic preparedness partnership, there is also scope for inviting ad hoc experts from various partnerships, including the UK. Voting members will be the Member States, but contributions and inputs from the UK and other stakeholders will be integral to shaping the subgroup's recommendations and ensuring broad-based support and collaboration across borders.

European warm-base Laboratory Networks

LAB-Net

Surbhi Malhotra-Kumar - University of Antwerp, Belgium

Prof. Surbhi Malhotra-Kumar opens her presentation on LAB-Net by emphasizing the pivotal role that laboratories play in the clinical trial infrastructure. LAB-Net, a globally coordinated network of laboratories, aims to mitigate the burden of infectious diseases and enhance pandemic preparedness. The network operates with three core activities: providing trial services, aiding in diagnostic testing, and biobanking samples.

Trial services

LAB-Net's trial services encompass comprehensive support from the inception of clinical trials to their conclusion. This includes developing lab protocols, training laboratories, and conducting final analyses. The network supports both academic and industry-based research. Additionally, LAB-Net assists in selecting Contract Research Organizations (CROs) and diagnostic tests, site selection, and study-specific training. The network ensures uniformity and quality across all participating clinical labs through external quality assessment panels, Good Clinical Laboratory Practice (GCLP) training, and constant feedback mechanisms.

Diagnostic testing

In the realm of diagnostic testing, LAB-Net contributes to the development, evaluation, and application of diagnostic assays. The network's involvement in the COMBACTE studies with AstraZeneca exemplifies its role in validating diagnostic tests for clinical trials. LAB-Net validated and implemented GeneXpert tests by CEPHEID in trials targeting *Pseudomonas* and *Staph aureus* colonization.

Biobanking

LAB-Net manages an extensive biobank housing over 170,000 infectious disease samples and an equal number of isolates. The biobank includes One Health biological specimens spanning veterinary, animal, environmental, and human clinical samples, all linked to relevant clinical data. This vast repository supports a wide range of stakeholders, including pharmaceutical companies, SMEs, universities, NGOs, and European clinical trial networks.

Network structure and coordination

LAB-Net's global reach spans 75 countries, with 41 European countries and 34 non-EU countries actively participating. The network comprises 925 routine microbiology labs, 16 research laboratories, and additional labs ready for deployment as needed. The University of Antwerp's Laboratory of Medical Microbiology (LMM) functions as the central coordination centre, ensuring efficient management and swift response times.

Laboratory types and roles

LAB-Net encompasses three types of laboratories: routine diagnostic labs, the central laboratory in Antwerp, and specialized research laboratories. Routine diagnostic labs handle sample and strain collections, testing, and storage. The central laboratory prepares and ships study materials, creates sample kits, biobanks samples, and provides training. Specialized laboratories perform exploratory work on specific samples or strains and may also engage in biobanking.

Training and education

LAB-Net places a strong emphasis on training and capacity building. The network offers study-specific diagnostic support, capacity-building activities, and plans to introduce performance-based webinars for continuous technical and laboratory education. The GCLP training and the provision of lab manuals and protocols further reinforce the standardization and quality of laboratory practices within the network.

Collaborations and future directions

With over a decade of experience, LAB-Net has supported more than 50 clinical trials involving samples from over 31,000 patients across 46 countries. The network collaborates with a diverse array of partners, including pharmaceutical companies, academic institutions, and non-profit organizations. LAB-Net's integration into ECRAID and its memorandums of understanding with PENTA and GARDP highlight its strategic partnerships and preferred lab status. Looking ahead, LAB-Net aims to expand its virtual biobank capabilities, enhancing accessibility and management of biobanked samples. The network's ongoing efforts to integrate and train laboratories worldwide ensure it remains at the forefront of clinical trial support and infectious disease research.

In conclusion, LAB-Net's comprehensive and coordinated approach, extensive biobank, and robust training programs make it an indispensable component of the global clinical trial infrastructure, driving advancements in infectious disease research and pandemic preparedness.

Discussion and comments

On sample sharing procedures

Surbhi Malhotra-Kumar (University of Antwerp): Since the GRACE project, various consortia have operated under distinct rules for sharing samples. LAB-Net aims to streamline this process by developing metadata catalogues available on the BBMRI-ERIC website, facilitating easier access and contact for sample requests. Although projects still adhere to their specific rules, LAB-Net plans to establish a uniform approach for sample sharing. Upon receiving a sample request, LAB-Net contacts the project's Coordination Committee to approve the release of samples. Additionally, LAB-Net is exploring a federated approach for sample visitation, allowing data analysis without direct access to the samples.

Evelina Tacconelli (University of Verona): A significant improvement in sample sharing and data management was achieved by implementing a dedicated team for data centralization and monetization. This system was particularly successful in ORCHESTRA, a large project that managed 60,000 samples over four years, linking clinical, epidemiological, and microbiological data with a unified code across Europe. This system, developed by Cineca along with other project partners and integrated into the work performed by the UAntwerp teams (who are the central lab for ORCHESTRA), enables precise tracking and data linkage, greatly enhancing the ability to address scientific inquiries.

DURABLE

Christian Drosten - Charité Berlin, Germany

DURABLE is a research-centric network composed mainly of academic institutions across various countries, funded by HERA for four years with a 25 million euro grant. The network includes 20 institutions and about 170 individuals, focusing on preparedness research during early pandemic phases, ranging from diagnostics to preclinical vaccine and drug development.

The organizational structure of DURABLE is divided into work packages, one of which is specifically designed for emergency response. It facilitates frequent meetings and information exchanges among network members, allowing for timely responses to current issues like the H5N1 virus. The network's geographical distribution covers major European academic players and public health institutions, ensuring robust collaboration and research output.

One significant aspect of DURABLE is its One Health approach, integrating veterinary and human public health efforts, which has already proven beneficial in research activities related to H5N1. The network's global health arm is managed through the Pasteur Network, which aids in overseas pathogen research and surveillance.

DURABLE's research efforts are diverse, including the development of diagnostic tools for viruses like Filoviruses, Mpox, and H5N1. These tools are created and quality-controlled within the network's labs to ensure readiness for emergencies. Another research area focuses on aerosol biology and pathogen transmission, addressing how pathogens are dispersed through the air and their stability in aerosols. Additionally, the network studies vector distribution, particularly in southern Europe, concerning pathogens like Ebola and West Nile viruses.

The network also investigates population-level immunity, exploring whether exposure to circulating influenza viruses pre-immunizes populations against H5N1. This research includes analysing the evolution of antigenicity in pathogens like SARS-CoV-2 to inform vaccine development and adaptation. Finally, DURABLE fosters virus phenotyping to understand the functional implications of genetic sequences, a need highlighted by the COVID-19 pandemic. This includes studies on virus behaviour and characteristics beyond mere sequencing, which is crucial for comprehensive pathogen understanding.

European warm-base Clinical Trials Networks

European Clinical Research Alliance on Infectious Diseases (Ecraid)

Evelina Tacconelli - CSO Ecraid

Prof. Evelina Tacconelli outlines the significant history and strengths of Ecraid, emphasizing its foundation on robust collaboration among partners in COMBACTE and PREPARE, resulting in a comprehensive clinical research infrastructure consisting of four high-quality networks: CLIN-Net (hospital and primary care network), LAB-Net (laboratory networks), STAT-Net (statistical support), and EPI-Net (epidemiological surveillance). Ecraid's journey began with targeting antimicrobial-resistant infections, through projects like MOSAR, SATURN, R-GNOSIS, and emerging infectious diseases caused by viruses like PREPARE.

Ecraid has a Coordination Committee that recently included expertise in data monetization and storage, aiming to enhance research dissemination and engage Eastern European sites. A new pharmacological pillar was introduced to handle study-specific requirements, and a clinical liaison in each country was appointed to address national needs. Patient organizations were also integrated, reflecting Ecraid's commitment to public engagement.

Ecraid operates as a nonprofit organization with a Management Board and a Supervisory Board. Its unique structure includes local support units and clinical liaisons across Europe. Prof. Tacconelli highlighted three core capabilities of Ecraid: enrolling patients for randomized clinical trials, maintaining active prospective cohorts, and providing rapid research responses in pandemic scenarios. The network boasts over 1,200 hospitals in 42 countries, 900 labs, 300 primary care sites, and multiple specialized sites for children, pregnant women, and long-term care facilities.

The site selection process in Ecraid is meticulous, ensuring that participating sites are committed to infectious disease research. This process includes capability assessments and lab qualifications, supported by the Ecraid clinical liaison council. Sites can also join by contacting national representatives. The current study portfolio includes randomized clinical trials, cohort studies, and surveillance systems like SAATELLITE2.

Ecraid's perpetual observation studies span 173 cohorts in 24 countries, focusing on ICU, primary care, emergency rooms, and hospital wards. These studies target diseases like ventilator-associated pneumonia, complex urinary tract infections, and acute respiratory tract infections, utilizing a standardized protocol across multiple sites. The organization has seen significant patient enrolment growth, to more than 18,000 patients in recent months.

Ecraid emphasizes effective data management through a dedicated interface that allows data to stay within the country while sharing on a common platform. Countries can access their data, propose new studies, and contribute to disease burden assessments. The organization collaborates globally, including with networks in Asia (ADVANCE-ID) and the US (ARLG), to enhance research capabilities and impact.

In a potential new pandemic scenario, Ecraid is equipped to provide rapid responses through active trials like REMAP-CAP and RECOVERY-EU. The organization's infrastructure supports long-term follow-up for randomized clinical trials and can adapt to emerging clinical scenarios. Ecraid's collaboration with ECDC highlights its role in public health, exemplified by its rapid response to the *Klebsiella* hypervirulent strain alarm.

Ecraid invests heavily in education, offering free webinars and training on topics like Urinary Tract Infections, lab reporting, study design, and data management. The organization values young and female researchers, participating in global initiatives and workshops to prepare for future pandemics. Prof. Tacconelli concluded by emphasizing Ecraid's commitment to transferring research findings to clinical practice and its ongoing contributions to public health and education.

EU-RESPONSE

Maya Hites and Inge Christoffer Olsen - Partners of EU- RESPONSE

In early 2020, the global medical community faced an urgent challenge to find effective treatments for the SARS-CoV-2 virus. The DISCOVERY platform trial began in France in March 2020 as a sister trial to the WHO SOLIDARITY trial, aiming to provide more detailed patient data. Shortly after, the EU-RESPONSE project was initiated, receiving financial support from the European Commission and involving 22 partners across 17 countries.

The primary objectives of EU-RESPONSE included expanding the DISCOVERY trial throughout Europe, establishing a multinational European multi-arm COVID-19 platform trial (EU-SolidAct), and developing a network of hospitals capable of conducting clinical trials for COVID-19 and other infectious diseases. By including over 1800 patients from 17 countries and 100 sites, the project successfully developed master protocols for phase II and phase III trials. These efforts yielded significant scientific findings, particularly in supporting the WHO SOLIDARITY trial and providing granular data on repurposed drugs and treatments like remdesivir and baricitinib.

EU-RESPONSE contributed to understanding the viral kinetics, the effects of different antivirals, and the cardiac events in remdesivir-treated patients. It also emphasized the inclusion of immunocompromised patients in COVID trials and the necessity of accelerating clinical trial implementation for future pandemics. Through advocacy, the project highlighted the challenges faced, lessons learned, and recommendations for future clinical trials, emphasizing quality control and pharmacovigilance during a pandemic.

Although patient inclusion in clinical trials has ceased, the project continues through biobanking and ongoing ancillary studies aimed at further exploring host and pathogen responses. An unintended yet beneficial outcome was the establishment of VIRvOLT, a network of virology reference laboratories designed to standardize and compare virological results across European centres, enhancing preparedness for future infections.

Challenges and strategic planning for the future

Dr. Inge Christoffer Olsen discussed the future of EU-RESPONSE, comparing its current state to Ecraid 10-15 years ago. The challenge lies in transforming the project-based network into a permanent structure. Questions arose regarding the type of network needed, whether it should focus on a broad range of infectious diseases or specialize, and how to balance the inclusion of repurposed and novel drugs.

The consortium has decided on a syndromic approach for future trials, targeting patients with general viral respiratory tract infections. This approach could easily pivot to address new emergencies, particularly if they involve pulmonary virus infections. The proposed EU PROACT project, submitted for the EU Horizon Europe call, aims to conduct both phase II and phase III trials during peacetime, which can be swiftly adapted in an emergency setting. (Post-meeting note: the EU PROACT project has been selected for funding)

Conclusion

The EU-RESPONSE project has made substantial progress in clinical trial protocols and network establishment, providing valuable insights and data. Moving forward, the focus will be on consolidating the network, ensuring its flexibility and preparedness for future pandemics, and determining the most effective strategies for clinical trials and patient care. Input from various stakeholders will be crucial to guide the project's evolution and success.

Discussion and comments

Herman Goossens (University of Antwerp) emphasizes the importance of developing a clear vision to build a clinical trial network, reflecting on similar discussions from 2016. He advises utilizing existing protocols, such as those from the University of Antwerp, for biobanking and sample sharing, advocating for collaboration to avoid redundant efforts and ensure alignment and harmonization within the project.

Evelina Tacconelli (University of Verona) questioned whether adaptive platform trials should target specific diseases or integrate multiple aspects. She expressed concern about limiting the scope to specific targets, like viral diseases in community-acquired pneumonia, and suggested leveraging broader networks for a more comprehensive approach.

Maya Hites (EU-RESPONSE) agreed with the need for collaboration and comprehensive approaches, highlighting discussions on expanding beyond viral respiratory infections to include antimicrobial resistance (AMR). She advocated for readiness to respond to various pandemics and emphasized the necessity of working together across different clinical trial groups.

Dirk Ramaekers (Belgian Ministry of Health) raised concerns about the overwhelming number of antiviral options during the COVID-19 pandemic and the need for more targeted interventions. He stressed the importance of investing in research and development for new medical countermeasures, such as antibiotics for AMR, and questioned the focus of future clinical trials. In response, Maya Hites discussed plans to evaluate broad-spectrum antivirals for respiratory infections, collaborate with labs and pharmaceutical companies on drug development, and ensure regulatory compliance. She highlighted the potential of existing drugs like remdesivir to offer partial effectiveness early in pandemics, buying time for the development of vaccines and monoclonal antibodies.

Marco Cavaleri (European Medicines Agency) proposed a modular approach to maintain a warm-base network, facilitating readiness for future pandemics. He suggested federating across networks to conduct trials for pathogen-agnostic treatments, using existing master protocols to generate useful evidence and ensure preparedness without isolating EU-Response from other networks.

PENTA - C4C

Carlo Giaquinto - Coordinator of PENTA and C4C

PENTA, or the Paediatric European Network for Treatment of AIDS, was established over 30 years ago in response to the inability to run clinical trials for children with HIV in Europe. Initially a spin-off from the European Collaborative Study on vertical transmission of HIV, PENTA has always emphasized a multidisciplinary, multinational approach combining cohorts, clinical trials, basic science, and social science to address the needs of children and families affected by HIV.

The organization's journey began with PENTA 1 in 1991, a randomized placebo-controlled trial on antiretroviral therapy (ART) versus placebo in children with HIV. Over the years, PENTA expanded its scope and in 2004, the PENTA Foundation was established, marking a significant organizational breakthrough. This allowed for more efficient management of international research and funding. Today, PENTA operates globally with over 600 members in 90 countries, 100 sites and partners in 42 countries, and strong collaborations with academia, regulatory authorities, and industry stakeholders.

PENTA's operations are robust, involving a network of clinical trial units in London, France, Thailand, and Spain, and a wide array of thematic working groups focusing on various paediatric infectious diseases. These groups address issues such as pregnancy and vertical transmission, blood-borne diseases including HIV, respiratory infections, fungal infections, and antimicrobial resistance (AMR). PENTA has also developed cross-cutting areas in basic sciences, PK, training and social sciences. Their business model ensures they retain ownership of the data from their studies, allowing them to support paediatric drug registration and answer strategic questions critical for child and maternal care.

The Foundation's impact is substantial, having contributed to the registration of several antiretroviral drugs. Notably, the Odyssey trial led to the global adoption of dolutegravir for children with HIV. PENTA has conducted 35 major clinical trials, enrolling over 50,000 women and children, primarily in low and middle-income countries. A significant achievement is the establishment of the pan-European paediatric clinical trials infrastructure, known as C4C, which facilitates the development of medicines for children.

In response to emerging health challenges and triggered by the SARS-CoV-2 outbreak, PENTA has been actively involved in pandemic preparedness. They have established cohort collaborations, adaptive clinical trial platforms in Africa for neonatal sepsis, and are leveraging the C4C network for rapid trial activation. PENTA's public-private funding model allows for flexibility and sustainability in their projects, ensuring continued support for critical programs even after initial funding ends.

Looking ahead, PENTA plans to engage in product development projects like Prometheus, which involves the development and testing of monoclonal antibodies for children and pregnant women. They are also working on a preparedness platform for pregnancy and infant health, with a focus on testing interventions for Respiratory Syncytial Virus (RSV). The foundation's evolving pipeline includes several innovative projects aimed at enhancing paediatric and maternal health globally.

VACCELERATE

Oliver Cornely - Coordinator of VACCELERATE

The VACCELERATE project focuses on enabling vaccine trials in Europe. Its five pillars are clinical trials, the Volunteer Registry, the Site Network, the VACCELERATE Academy, and pandemic preparedness.

VACCELERATE has run three major clinical trials: the AGED study, the BOOSTAVAC study, and the CoVacc study. The AGED study (sponsor: University Hospital Cologne) is notable for being the only randomized clinical trial focused on individuals aged 75 and older, and for being one of the very few studies comparing the two mRNA vaccines head-to-head. The BOOSTAVAC study (sponsor: University College Dublin), and the CoVacc study in children (sponsor: UMC Utrecht), also contribute valuable insights, although the latter faced challenges due to existing recommendations for COVID-19 vaccination of children, interfering with the study question.

The Volunteer Registry is an innovative aspect of VACCELERATE, active in 25 countries and supporting an international database of volunteers ready for clinical trials. This registry, available in 22 languages, facilitates faster trial initiation by having pre-registered volunteers, and it can be used for various vaccine-preventable or respiratory diseases, not just COVID-19.

The VACCELERATE Site Network includes 491 clinical trial sites across Europe and beyond, extending to 59 countries. This extensive network supports both adult and paediatric trials and collaborates with other networks like C4C and PENTA. The VACCELERATE Academy aims to enhance the capabilities of these sites, offering a structured pathway for trial sites to progress from basic to advanced levels of expertise through education and certification programs.

Pandemic preparedness is an additional task for VACCELERATE, in collaboration with the European Commission, which consists of six specific objectives. These include integrating into the European Pandemic Preparedness Partnership, intensifying collaboration with CoMeCT, liaising with the upcoming HERA subgroup, contributing to the ACT-EU initiative, developing the concept of preparedness trials for vaccines, and organizing a tabletop exercise for pandemic emergencies. These efforts are intended to enhance readiness for future pandemics and ensure that the network remains active and effective between pandemics.

Sustainability beyond the current funding period, which ends in January 2025, is a major focus of VACCELERATE. The consortium is developing a business plan and considers the creation of a new legal entity to streamline operations and ensure the continuity of the VACCELERATE clinical trial network. Key features of the future network include a focus on pandemic preparedness, meeting the needs of the vaccine trial community, transparent and participatory decision-making, lean and cost-effective operations, participation in both academic and industry-sponsored trials, and a preference for innovative trial methodology. The goal is to maintain an ever-warm network ready to respond in an emergency that can also answer important questions between pandemics, ensuring a return on investment and continued relevance.

The Coordination Mechanism for Cohorts and Trials (CoMeCT) - Linking cohorts and clinical trials

Victoria C. Simensen - NIPH, Norway & Evelina Tacconelli - University of Verona

Dr. Victoria C. Simensen, the coordinator of the Coordination Mechanism for Cohorts and Trials (CoMeCT), introduces this CSA project by explaining its unique model as a "network of networks." CoMeCT is funded by the Horizon Health HORIZON-HLTH-2023-DISEASE-03-05 program and is coordinated by the Norwegian Institute of Public Health. It involves the experienced partners Ecraid, ECRIN, University of Verona, INSERM, PENTA, and the University of Cologne. The project has a funding of 3 million Euros, with plans to continue until December 2026. A sustainability plan is included to ensure the longevity of these coordination efforts beyond the project period. One of the main goals is to align and expand the Trial Coordination Board (TCB) and Cohort Coordination Board (CCB) into a common Coordination Board and include an Outbreak Response Board (ORB). Additionally, the already established Joint Access and Advisory Mechanism (JAAM) will be strengthened to assess suitability of compounds beyond the scope of COVID-19. The JAAM also aspires to assess vaccines for further assessment in academic trials.

Dr. Simensen provides an overview of the project's Work Packages (WPs), emphasizing the key role of the Coordination Board (WP1) as the portal to the CoMeCT activities. The other WPs will focus on more technical aspects of coordination and feed their output to the Coordination Board. Such aspects are to facilitate for data reuse, adoption of data standards and data harmonization across studies, information sharing between investigators and the broader stakeholder landscape, and mapping of networks.

Dr. Simensen describes the background model for CoMeCT, rooted in the shared WP established by the EU-RESPONSE and RECOVER projects in 2020. This WP fostered the establishment of the TCB, the JAAM, and the APT Toolbox enabling dialogue and collaboration between Adaptive Platform Trials (APTs) and the broader landscape.

Over the past four years, the TCB has grown, incorporating the EU-funded projects VACCELERATE, ECRAID-PRIME and MPX RESPONSE, thus expanding scope to include outpatient trials, vaccine trials and pathogenic focus of trials. The TCB now comprises founding members, all partners of CoMeCT, representatives from the Commission (RTD, HERA, HaDEA) and EMA, and various EU-funded and global trial investigators. Dr. Simensen highlights the value of the continuous discussions with stakeholders such as ECDC, WHO, CEPI, and health technology assessment agencies, which have been pivotal in harmonizing protocols, accelerating trial approval processes, and discussing results (further sub-analyses, metanalyses, and implications for guidelines and clinical care). The discussions have also contributed to a more integrated policy landscape.

Through the Coordination Board, CoMeCT aims to set up an Outbreak Response Board, tasked with developing scientific criteria for early research response and ensuring evidence synthesis and transmission. The Coordination Board in CoMeCT aspires to act as a central scientific advisor to other European Coordination entities such as the European Pandemic Preparedness Partnership and the HERA Board Subgroup for clinical trial prioritizing and funding. As the current coordination landscape is evolving, roles and organization are yet to be defined. Feedback on coordination experience has shown that current structures are trusted but have lacked optimal impact, and that prospective coordination is easier to achieve if working with more authoritative entities.

The second speaker in this session, Prof. Evelina Tacconelli, discusses the current European cohort landscape, the role of the Cohort Coordination Board (CCB), and the important role that should be given to cohorts in pandemic preparedness plans. She highlights the importance of observational study data in informing randomized clinical trials (RCTs) and emphasizes that this interplay should be progressed. She emphasizes the role of cohorts in targeting populations that are underserved in the research field such as children, elderly, pregnant women, as well the medically vulnerable populations (oncological, post- transplant patients).

Prof. Tacconelli points out the ORCHESTRA project as a successful cohort project, funded with 30 million euros and enrolling 528,000 patients since 2021. This project includes 82 different cohorts, covering diverse populations such as healthcare workers, patients with long COVID, and vulnerable populations. The ORCHESTRA project operates a web-based data portal, centralizing information from various European countries while respecting different data dictionaries and ensuring data standardization across cohorts. The data is pseudo-anonymized and accessible for federated data analysis, preventing data from leaving the country of origin.

Prof. Tacconelli's presentation discusses the alignment of cohorts and trials through initiatives like CoMeCT. Prof. Tacconelli emphasizes the importance of building and exploiting a central data repository for mapping metadata from trials and cohorts, enabling researchers to use standardized data dictionaries.

The presentation addresses the need for a new clinical trials ecosystem that integrates results from cohort studies in the progress of a clinical trial. This model aspires the set-up of an ecosystem that supports pre-trial hypothesis generation, long-term assessment of interventions, and post-authorization safety monitoring. Prof. Tacconelli underscores the importance of harmonizing cohorts during pandemics to allow for rapid knowledge generation and subsequent response. She also advocated for using healthcare workers as a sustainable cohort due to their high-risk exposure and willingness to participate.

Prof. Tacconelli concludes by stressing the importance of continuous support for cohort studies beyond pandemic times to ensure a robust and adaptive clinical study ecosystem. She poses three questions for consideration: how to implement a new clinical study ecosystem, how to ensure sustainability, and how to reinforce the link between existing adaptive platform trials and cohort networks?

Discussion and comments

Patrick Mallon (University College Dublin) emphasizes the importance of cohorts in facilitating basic science discoveries necessary for clinical trials. He highlights how cohorts helped identify correlates of immunity for SARS-CoV-2, a process that took two and a half years. Mallon notes a gap in Europe's network of scientists capable of delivering quick diagnostic tools, stressing the essential role of cohort studies in advancing knowledge and diagnostics.

Evelina Tacconelli (University of Verona) responds by acknowledging these points and adding that APTs face limitations, particularly in terms of involving broader immunological expertise beyond infectious disease wards. She mentions efforts to engage internal medicine societies, subspecialties and immunology experts, using sepsis as an example where more expertise is needed. Tacconelli also notes the potential of biobanking from COVID-19 cohorts. These have collected numerous samples yet to be analysed, suggesting this as a foundational step toward future research and collaboration.

Inge Christoffer Olsen (EU-RESPONSE) emphasizes the importance of harmonizing data capture standards between APTs and cohorts to create a powerful and standardized system. He expresses enthusiasm for standardization and suggests that trialists should learn from cohorts and adopt the same standards.

Evelina Tacconelli responds by confirming that this harmonization is already being addressed in WP 3 and 4 of CoMeCT. She explains that they have a task focused on aligning cohorts and trials, which includes standardizing variables across languages. When working with leaders of randomized clinical trials, they can import the most important variables, ensuring comparable data and seamless linkage in trial designs.

European Partnership for Pandemic Preparedness

Laurent Jaboeuf – Project Officer BE READY

Laurent Jaboeuf's talk on the European Partnership for Pandemic Preparedness provides a comprehensive overview of the initiative aimed at bolstering the continent's readiness for future pandemics through research and innovation. The partnership's framework is currently being constructed under the BE READY CSA (Coordination and Support Action), involving 26 partners from 16 countries. The partnership's scope is specifically targeted at enhancing research and innovation related to pandemic preparedness. It aims to create a collaborative environment where the entire research community can work together effectively. This includes building and strengthening research through joint transnational cohorts and supporting the readiness of the research ecosystem, particularly by facilitating ever-warm clinical trials that can be rapidly deployed when needed.

A key aspect of the presentation is the introduction of BE READY Plus, the next phase following the initial BE READY framework. This phase is currently in preparation, with a call for proposals open until November 2024. The timeline indicates that the partnership is expected to officially begin by the end of the third trimester of 2025.
The presentation also outlines the new work packages, particularly highlighting one designed to create links with clinical trial networks. This initiative is vital for integrating various stakeholders and ensuring continuous support and connectivity with the broader research ecosystem. Jaboeuf stresses the importance of keeping the partnership manageable by maintaining entry points through national contact points and establishing direct links with existing initiatives. This approach aims to streamline communication and collaboration, particularly with networks like CoMeCT related to clinical research.

In summary, the European Partnership for Pandemic Preparedness is a strategic initiative focused on enhancing research and innovation to prepare for future pandemics. It involves a collaborative framework, strategic investments in research, and robust support for clinical trials and the broader research ecosystem. The partnership aims to align various stakeholders towards common objectives, ensuring a coordinated and effective response to pandemic challenges.

EU-FUTURE-ID database and EuCoReFund survey and interviews

EU-FUTURE-ID database, EuCoReFund survey & interviews: an introduction

Safia Thaminy – University of Antwerp

In the final talk on 14 May, Safia Thaminy introduces the scope and objectives of the research carried out in Antwerp to better support the coordination of clinical research in Europe during infectious disease outbreaks. She aims to explain the methodology, tools developed, and challenges faced with a more detailed presentation of the results scheduled for the following day.

At the workshop, 17 funding organizations from 10 countries that participated in the survey/interviews are attending the workshop, with additional participants joining online.

Onsite workshop participants

Austrian Research Promotion Agency	Austria
Ludwig Boltzmann Gesellschaft	Austria
Ministry of Education, Science and Research	Austria
Health Care Knowledge Centre	Belgium
Fund for Scientific Research	Belgium
Estonian Research Council	Estonia
INSERM	France
Federal Ministry of Education and Research	Germany
Deutsche Forschungsgemeinschaft	Germany
Netzwerk Universitätsmedizin	Germany
Health Research Board	Ireland
NordForsk	Norway
The Research Council of Norway	Norway
Swedish Research Council	Sweden
Tübitak	Turkey
Department of Health and Social Care	United Kingdom
National Institute for Health and Care Research	United Kingdom

Online workshop participants

European Joint Programme on Rare Diseases	France
Science Foundation Ireland	Ireland
Fondazione Cariplo	Italy
Institute of Public Health	Italy
Tuscany Region	Italy
Research Promotion Agency	Italy
National Centre for Research and Development	Poland
Agencia de Investigação Clínica e Inovação Biomédica (AICIB)	Portugal
Wallenberg Foundation	Sweden

Rationale and approach

The pandemic's surge in clinical research exposed gaps in coordination, prompting the need to streamline funding efforts for future pandemics. The national funders' role is crucial in this regard. The research initiated in Summer 2023 involved creating a comprehensive database of funding organizations in Europe, followed by a survey sent to the identified funding organisations and interviews to gather detailed information on their policies, funding mechanisms and responses during the COVID-19 pandemic.

Development of the EU-FUTURE-ID Database

EU-FUTURE-ID stands for 'EUropean FUnders of clinical studies, Trials and Urgent REsearch for Infectious Disease outbreaks'. The database was created to address the lack of comprehensive, up-to-date and publicly available resource on European funding organizations for infectious disease clinical research. Pre-existing global databases like PandemicTrack GLoPID-R are currently covering few European funders, thus necessitating a database specifically focused on funding organisations located in Europe. The development of the EU-FUTURE-ID database involved a multi-step approach:

- Creating a Working Group to define scope, eligibility, and strategy.
- Identifying funding organizations through predefined networks and desk research.
- Reaching the funding organisations by phone calls.
- Updating the database with feedback collected during interviews.

The database includes detailed profiles of funding organizations, including contact information and type of organization. However, maintaining up-to-date and accurate contact details remains a continuous challenge and an important point of attention to create a sustainable database in the future.

EuCoRefund Survey and interviews: approach and challenges

EuCoRefund stands for 'European COordination of Clinical REsearch Funding'. The survey aimed to collect information about the funding landscape before and during the pandemic notably by comparing the number and type of clinical studies funded and the budgets allocated. Despite initial low response rates to participate in this survey, follow-up phone calls significantly increased participation. The qualitative interviews that were organized with the organisations that participated in the survey provided deeper insights into the funding mechanisms, policies challenges faced by national funders during the COVID-19 pandemic.

Several challenges were highlighted:

- Identifying the right contact persons within the funding organizations
- Engaging funders to participate in survey and interviews.
- Variability in database structures and classification systems among funders.
- Sensitivity of requested data, such as budget allocations, and hesitancy to share such data.

Preliminary findings and future steps

Preliminary findings indicate diverse preparedness levels among funding organizations, with some relying essentially on ad hoc mechanisms and others undertaking internal evaluations to improve future responses. Safia Thaminy concludes with an overview of the planned discussions and case studies to be presented the next day, aiming to inspire deeper discussions on the funding landscape and coordination mechanisms for clinical research in Europe.

Discussion and comments

Ole Olesen (European Vaccine Initiative) suggests contacting Policy Cures Research, an NGO which has been collecting information about funding for infectious diseases globally: https://www.policycuresresearch.org/

EuCoReFund survey & interviews: preliminary results

Safia Thaminy – University of Antwerp

At the start of the second day of the workshop, Safia Thaminy presents the preliminary outcomes of the EuCoReFund survey and interviews, highlighting the complexities and challenges in coordinating public funding for clinical research across Europe.

Despite the challenge in engaging stakeholders and obtaining detailed data, particularly regarding the number of funded studies and budget allocations, most participating funders provided accurate information, facilitating a detailed analysis of the funding landscape and policies. A key finding highlighted through the interviews is the complexity of the clinical research landscape, with funding primarily coming from national sources and diverse departments, each with distinct organizational structures and mandates aligned with national or political interests. The lack of a holistic view of the funding landscape at the national level is noted as a significant barrier to effective coordination among different funders.

Survey results show that before the pandemic, 65% of the funders supported infectious disease research, which increased to 80% during the pandemic. This demonstrates a strong response to the crisis, with many funders adapting their normal schemes to rapidly support the clinical research response. However, resource prioritization was often ad hoc and lacked clear, transparent strategies, underscoring the need for more structured decision-making processes.
The data reveals a significant increase in observational studies funded during the pandemic in comparison to interventional studies. Overall, budget allocations also increased, particularly among organizations that generally dedicate modest budget before the pandemic. However, leveraging rapidly additional funds was challenging for many organizations, highlighting the necessity of identifying other funding sources and mechanisms for rapid response in future emergencies.

The analysis of multinational clinical studies reveals that 60% of funders did not support such studies during the pandemic, primarily due to limited experience and the preference for national studies. This point emphasizes the need for better strategies to engage funders in multinational efforts during peacetime and to overcome barriers to collaboration. The interviews also highlighted the importance of transitioning from competitive to collaborative funding models, strengthening communication among funders, and building trust through consistent and trustworthy collaborations.

Several key points are identified for improving coordination: enhancing communication among funders, diversifying funding mechanisms to adapt to different needs, ensuring transparent decision-making processes, and aligning rapid funding responses with system responsiveness. The need for quality and robust studies during outbreak diseases was also highlighted as a with clear criteria for funder participation in multinational studies. Safia Thaminy concludes with a call for concrete actions to support multinational clinical research, to enhance collaboration and improve responsiveness, ensuring preparedness and effective coordination in future health crises.

Discussion and comments

Simona Grasso (Research Council of Norway - RCN) reflects on their response to the COVID-19 pandemic, highlighting key learnings for future emergencies. RCN had to quickly establish two parallel processes: one to seek permission from ministries and other funders to reallocate emergency funds, and another to determine which types of research to fund. Effective communication with other European funders was lacking to avoid duplicating efforts and to align prioritization. In Norway, however, RCN received draft proposals and connected researchers when they saw that there was possibility for collaboration which resulted in stronger applications and broader networks. Grasso emphasizes the importance of establishing mechanisms for immediate activation during crises and ensuring the quality and robustness of funded studies, which she sees as a key responsibility of funders.

On the issue of rapidly releasing clinical trial funds during pandemic outbreaks

Oliver Cornely (University of Cologne) emphasizes the necessity for a rapid funding mechanism that can release substantial funds, such as 10 million euros, within days without extensive discussions. This immediate release is crucial for initiating work promptly. However, this approach requires a downstream organization capable of utilizing these funds effectively. He points out that while existing networks are in place to handle such rapid deployment, the typical procedure of issuing calls for proposals is ineffective in a crisis.

Herman Goossens (University of Antwerp) highlights the inadequacy of the current competitive funding mechanisms during pandemics. The process of publishing calls, selecting projects, and signing contracts is too slow. He acknowledges that RTD acted very quickly during the early days of the COVID pandemic, but emphasizes that a different, faster mechanism is needed for future pandemics.

There is a general agreement about the need for better exploitation of existing networks to enhance the efficiency of rapid funding deployment during crises.

On non-pharmaceutical interventions

Herman Goossens argues that, during the COVID-19 pandemic, numerous non-pharmaceutical public health interventions were implemented, but very few were evaluated for their effectiveness. This lack of evaluation leaves us largely unaware of which measures were successful. Norway is an exception, having conducted an evaluation. It is embarrassing that so many interventions were carried out in Europe and globally without assessing their impact, highlighting the need for better evaluation practices in the future.

Funding Mechanisms:
from theory to practice in four case studies

The EuCoReFund interviews revealed several compelling examples that highlight the obstacles, challenges, and potential solutions for coordinating the funding of clinical research and trials during pandemic outbreaks. Four standout cases have been chosen to showcase at the workshop, aiming not only to inform attendees but also to spark inspiration and drive discussions on creating a coordinated funding mechanism across Europe.

1. The BeNefit program for comparative effectiveness studies: a Belgian-Dutch collaboration

Frank Hulstaert - Belgian Healthcare Knowledge Center (KCE)

The BeNefit program is a collaborative initiative between the Belgian Health Care Knowledge Center (KCE) and the Dutch ZonMw, aimed at jointly funding non-commercial comparative effectiveness trials.

In 2016, prior to engaging in a collaboration with the Netherlands, KCE had launched a funding program for pragmatic comparative effectiveness studies, including the repurposing of out-of-patent drugs. This drug repurposing program was expanded during the COVID-19 pandemic, and proved very valuable as in the early days, there were no newly developed drugs for SARS-CoV-2. In this context, Frank Hulstaert highlights the quick response of Belgium in initiating COVID-19 trials, particularly a study on blocking Interleukin-1 and Interleukin-6, which moved from concept to patient enrolment in just two weeks. This rapid response was achieved through a consensus approach that combined top-down and bottom-up strategies, involving regulators, funders, payers, clinicians and clinical trial units.

The actual collaboration with the Netherlands began in 2017, when the BeNefit program was launched, aiming to conduct non-commercial comparative effectiveness trials across both countries, with a broader scope than pharmaceuticals, including devices, surgery, and other reimbursable interventions. It involves patients of both countries in the decision-making process and focuses on investigator-led trials. The program ensures the publication of all trial results, including negative outcomes, and emphasizes data sharing. Of note, Hulstaert stresses the importance of regular collaboration among funders to improve funding practices and ensure high-quality, timely, and within-budget trials.

The cross-border BeNefit collaboration includes a common management team, a joint application portal, and a unified selection process. However, differences between the two countries, such as healthcare system variations and budget management, present challenges. For instance, Belgium operates with a yearly budget, while ZonMw uses a per-call budget system, which Hulstaert notes is more conducive to running trials. Additionally, there are differences in protocol improvement efforts, conflict of interest handling, and the intensity of trial follow-up between KCE and ZonMw.

Despite these challenges, the BeNefit program has successfully launched three calls for proposals in six years, with a fourth under discussion. The collaboration between Belgium and the Netherlands represents a significant effort to combine the strengths of both countries' approaches to clinical trials, with the goal of improving healthcare outcomes through well-designed, non-commercial trials that would be difficult to conduct in a single country.

Discussion and comments

On the role of non-university hospitals

In the BeNefit collaboration between KCE and ZonMw, while initial consultations were primarily with legal experts from university hospitals due to their greater experience, the program also values and includes non-university hospitals in clinical trials. Although non-university hospitals had to align with the consensus reached by university hospital legal experts, some of the most successful trials have been led by large non-university hospitals, highlighting their significant contribution to the program.

On reducing bureaucratic hurdles for comparative effectiveness trials

Chris Butler (University of Oxford) emphasizes the need to reduce the cumbersome regulations surrounding comparative effectiveness trials, especially when these trials involve low-risk scenarios, such as choosing between two licensed medications. He points out the irrationality of current regulations where a general practitioner (GP) could randomly choose a treatment without facing consequences, but would face legal issues if they randomized a patient as part of a trial, even though this would generate valuable data. Butler suggests that reducing bureaucratic hurdles would make it easier to conduct quicker, larger, and more efficient trials, ultimately benefiting patient care.

Frank Hulstaert (Belgian Healthcare Knowledge Center - KCE) agrees with this point, particularly in the context of more established treatments rather than early-phase pandemic trials. He notes that while the Netherlands has successfully reduced administrative burdens for low-risk, low-intervention trials, Belgium's regulators have been more cautious and less willing to ease these requirements. Hulstaert acknowledges the importance of streamlining the process for pragmatic, low-risk trials to allow for faster approvals and implementation, thereby facilitating more effective comparative effectiveness research.

2. The Nordic model for funding joint clinical research

Arne Flåøyen – NordForsk

Arne Flåøyen, the director of NordForsk, provides an insightful overview of the NordForsk model for funding research collaboration across the Nordic region. This region, comprising five countries and three self-governed regions with a combined population of 27 million, is highly integrated and boasts a significant global economy. NordForsk is an institution under the Nordic Council of Ministers, facilitating and funding research across various domains, from basic to applied research. Despite being small, with an annual turnover of around 30 million euros and only 16 staff members, NordForsk is described by Flåøyen as a "little red Ferrari"—highly visible, agile, effective, and wanted.

NordForsk's model is unique in that it requires co-funding from at least three Nordic countries to open a call for research proposals. The funding process is highly collaborative, involving national research funders who help design the calls based on their own national priorities. This model ensures that projects funded by NordForsk are truly reflective of regional needs and priorities. A significant requirement for any research project funded through NordForsk is that it must involve partners from at least three different Nordic countries, promoting regional cooperation and the pooling of resources.

A key aspect of NordForsk's operations is the emphasis on Nordic added value, which includes improved scientific quality through cross-border collaboration, enhanced regional mobility and networking, and the development of critical mass in specialized research areas. The model also offers cost efficiencies by sharing infrastructure and data, particularly the valuable Nordic health data registers. The common pot funding model used by NordForsk does not guarantee a fair return to each contributing country, but over time, all countries tend to benefit from the collaborative approach.

Flåøyen also highlights the flexibility of the NordForsk model, which can accommodate collaborations with non-Nordic countries, such as the Baltic states. Trust among national funders and a streamlined administrative process are critical success factors, making the NordForsk model both efficient and effective in managing and distributing research funds.

In reflecting on the COVID-19 pandemic, Flåøyen notes that while Nordic countries invested significantly in research, there was little cross-border collaboration, revealing a need for improved mechanisms for rapid response to future crises. In its latest, recently launched call, NordForsk is addressing this by funding networks focused on preparedness and resilience, aiming to create structures that can quickly mobilize in response to emergencies. This forward-looking approach aligns with the broader priorities of the Nordic Council of Ministers, which now emphasizes societal security across various domains, including health, cybersecurity, and climate change adaptation.

Recommended literature

- Nordic co-operation will pave the way for better health emergency preparedness – online article by Arne Flåøyen
- Funding for COVID-19 related research in the Nordic countries 2020-2021 – NordForsk report

Discussion and comments

Carlo Giaquinto (PENTA Foundation): *Do you receive funding from other sources like the Novo Nordisk Foundation? Given your robust mechanism, it seems attractive for external funders to participate.*

Arne Flåøyen (NordForsk): We've attempted to secure such funding but haven't been successful. Many foundations have statutes restricting their funds to their own country and researchers, and some prohibit collaboration with other funders. Novo Nordisk is a bit different—they could collaborate—but even after multiple discussions, they've opted to use their substantial resources, amounting to 1.2 billion euros, through their own channels.

Ole Olesen (European Vaccine Initiative): *Your model appears fantastic—low bureaucracy and highly efficient for Nordic collaboration. So why do the affluent Nordic countries allocate only 30 million euros to this mechanism? Why not invest more?*

Arne Flåøyen: It's a matter of decision-making structures. In Norway, the Research Council makes strategic funding decisions. However, in Sweden, a council of professors, who tend to be nationally focused, prefer to keep funds within their borders. They're hesitant to allocate money internationally. Finland shares a similar stance. Essentially, these boards prioritize national interests, favouring their own mechanisms over international collaboration.

Frank Hulstaert (Belgian Healthcare Knowledge Center - KCE): *In Belgium and the Netherlands, we utilize comparative effectiveness data within our healthcare systems, linking it to national patient numbers, hospitalizations, and billing data. This allows for long-term follow-up and supports Health Technology Assessments (HTA). Does NordForsk operate similarly?*

Arne Flåøyen: Our researchers report through Researchfish, and our only additional criterion to the general Researchfish criterions is the 'Nordic added value.' We focus on showcasing research impact through data and storytelling. However, the rights to the data reside with the researchers and their institutions; we're merely public funders. We do mandate that data adhere to the FAIR principles—Findable, Accessible, Interoperable, Reusable—as stipulated in our contracts promoting open science and open data. But we don't hold any direct rights to the data.

"The NordForsk model could be a great source of inspiration for the future pandemic preparedness partnership. There are definitely some compelling ideas there that could shape our approach moving forward. One key takeaway we've heard time and again: funders must meet regularly, build trust, and then collaborate. This step is absolutely vital." – Herman Goossens, University of Antwerp

3. The UK approach

Kate Gerrand - Department of Health and Social Care and Mike Rogers - National Institute for Health Research Coordinating Centre (NIHR)

In their session, Kate Gerrand and Mike Rogers present a detailed overview of the UK's approach to funding clinical research during the COVID-19 pandemic, highlighting the role of the National Institute of Health and Care Research (NIHR) and their rapid response mechanisms.

Kate Gerrand begins by introducing the NIHR, emphasizing its position as one of the largest health research funders in the UK, with a focus on applied research in healthcare and social care settings. The NIHR has a comprehensive infrastructure that supports high-quality research, invests in people, and fosters public and patient involvement. Gerrand notes that the success of the UK's COVID-19 research efforts was largely due to the pre-existing infrastructure, which was able to pivot quickly to address the pandemic's needs. The NIHR supported over 2 million participants in COVID-19 studies, utilizing innovative methods like platform trials, decentralized trials, and remote patient monitoring. Gerrand also mentions the NIHR's future plans, which include continuing collaboration with various stakeholders and enhancing pandemic preparedness.

Mike Rogers provides a more in-depth account of the specific actions taken during the pandemic. He explains that the NIHR had to adapt its usual funding processes to a more responsive model to meet the urgent demands of the pandemic. The three key areas of focus were speed, volume of information, and simplifying the application process. In February 2020, the NIHR, in collaboration with the Medical Research Council (MRC), launched a rapid response funding call. This initiative was split into two phases: the first focused on immediate therapeutic and vaccine interventions, with researchers given just nine days to apply, and the second phase, which allowed more time for other types of research, led to 26 awards, including funding for the Oxford vaccine and the PRINCIPLE trial.

Rogers emphasizes the importance of the NIHR's flexible and rapid funding approach, which was critical in addressing the acute phase of the pandemic. The COVID-19 Rolling Call allowed researchers to apply whenever they were ready, streamlining the process further. The call received over 700 applications, marking it as the busiest in NIHR's history. Rogers highlights the essential role of the Clinical Research Network in delivering funded research across the NHS and other health and care settings, which became particularly crucial during the pandemic. The network's urgent public health (UPH) designation helped prioritize resources and expedite regulatory processes, enabling rapid study implementation, such as the RECOVERY trial, which began recruiting patients just two weeks after receiving funding.

Finally, Kate Gerrand concludes by discussing how the lessons learned from the pandemic are being embedded into future research funding and delivery frameworks. The NIHR is developing a cross-UK research funders framework focused on pandemic preparedness and response. This includes commissioning pandemic research, expanding rapid evaluation capabilities, and continuing to prioritize public and patient involvement. Additionally, the NIHR is working on improving commercial clinical trials in the UK and is actively engaged in international collaborations to enhance global preparedness for future health threats.

Discussion and comments

Herman Goossens (University of Antwerp) criticizes the lack of top-down support for the REMAP-CAP trial in the EU during early 2020, contrasting this with the success in the UK, where both top-down and bottom-up support existed. He notes that EU Member States were not encouraged to participate, and that the SOLIDARITY trial was launched in competition with REMAP-CAP, which further fragmented essential research. Although the EU eventually provided an additional €15 million of funding in June 2020 for REMAP-CAP, Goossens emphasizes that successful trials require political support at both the top and grassroots levels, as was evident in the UK.

Frank Hulstaert (Belgian Healthcare Knowledge Center - KCE) highlights the relatively low budget for large trials in the UK and emphasizes the importance of the UK's additional 350 million pounds for structural support, such as study nurses and clinical trial units, which he believes was crucial to the success of these trials. He contrasts this with Belgium's experience, where attempts to join the PANORAMIC trial failed due to high administrative burdens and a lack of infrastructure. Hulstaert also notes the challenges of expanding into early-phase trials due to legal complexities and the need for extensive legal expertise, which the UK possesses.

Carlo Giaquinto (PENTA Foundation) praises the UK's foresight in developing clinical trial infrastructure around hospitals over the past 20 years. He particularly commends the UK's paediatric network, which is unique in its integration with paediatric wards and hospitals rather than just academic institutions. Giaquinto acknowledges that this infrastructure has contributed significantly to the UK's efficiency in managing funding mechanisms.

Mike Rogers (NIHR) emphasizes that competitive calls for research funding can be effective, as seen in the UK's approach. However, he argues that vaccines might require a different approach. He notes that the success of the Oxford vaccine during the COVID-19 pandemic was largely due to pre-existing work by Sarah Gilbert on a MERS vaccine, which was quickly adapted to target COVID-19. He believes that while competition drives excellence, vaccine development may need more strategic planning, given its unique challenges.

Kate Gerrand (UK Department of Health and Social Care) discusses the development of the vaccine research registry during COVID-19, similar to VACCELERATE's newly established volunteer registry. This registry allowed for rapid recruitment of participants for vaccine trials, with half a million people signing up in 2020. This efficiency enabled the quick recruitment for the Novavax trial in the UK. Gerrand explains that the vaccine research registry has since evolved into a broader platform called "Be Part of Research," which notifies participants about various research opportunities in their areas of interest through a regular newsletter. This initiative continues to be successful.

4. The German approach to coordinating clinical COVID-19 research: the Network of University Medicine (NUM)

Ralf Heyder - Netzwerk Universitätsmedizin (NUM)

Ralf Heyder discusses the German Network of University Medicine, a collaboration among all 36 German academic medical centres, which represent about 10% of the country's acute inpatient care. Established in response to the COVID-19 pandemic in April 2020, the network was created after the federal government realized Germany's lack of national coordination in clinical data and research efforts.

Funded with a €390 million federal grant over five years, the network aims to address these gaps by fostering large, multicentre research projects and developing critical research infrastructures.

The network operates from a Coordination Office at Charité in Berlin and manages a portfolio of 24 multicentre projects, with participation from at least 12 and up to all 36 sites per project. The projects are categorized into two types: infrastructure projects, which build and maintain research and data infrastructures, and research projects, which use these infrastructures to address specific scientific questions. This approach positions the network not only as a funder but primarily as a provider of clinical research infrastructure across Germany.

Governance of the network is highly decentralized, with leadership distributed among 21 different sites, and decision-making largely within the research community. However, a top-down governance structure is also in place, with a national task force comprising representatives from the Federal Ministries of Research and Health, as well as other key stakeholders. The Coordination Office liaises directly with local coordination units at each university medical centre, ensuring seamless operation and collaboration across the network.

Strategically, the network focuses on three main goals: establishing a national "one-stop-shop" for clinical research coordination, improving pandemic and crisis preparedness through surveillance and rapid response platforms, and creating a comprehensive clinical research data space for Germany. The latter involves building modular platforms to handle various types of clinical data, such as routine data, bio-samples, imaging, and omics data, ensuring these platforms are interconnected to avoid siloed information.

Heyder highlights several ongoing projects, including NAPKON, a COVID cohort network, an autopsy registry that integrates data from multiple medical disciplines, and the RACOON imaging platform, which unites all 36 German radiology departments to standardize data collection for AI training and research. The network's approach to funding is non-competitive, encouraging collaboration among researchers to strengthen project outcomes. For example, when developing the RACOON medical imaging platform, two competing consortia from different regions were instructed to collaborate to secure funding. This strategy ensures that every proposal is backed by a strong, unified research community, increasing the likelihood of successful project implementation.

Looking forward, there are plans to institutionalize the network as a permanent federal institution, which would provide indefinite funding and facilitate its integration into international research efforts. This would ensure the sustainability and expansion of the network's infrastructures and its role in global research collaborations.

Discussion and comments

On the NUM's linkage with the healthcare payer system in Germany

Ralf Heyder (NUM): In Germany, we are facing a lack of coordination among the approximately 100 health insurance funds for providing data for research. Currently, researchers must individually contact each fund to access data, which is impractical for most projects. To address this, efforts are underway to aggregate and link the data from these funds on a centralized platform. While progress is being made, the system is not yet fully operational. Once established, this platform will hopefully facilitate collaborative studies with insurance funds, particularly to quickly generate evidence on new treatment options.

On the role of the local coordination units

Ralf Heyder (NUM): Local coordination units essentially provide administrative support to researchers by helping them navigate bureaucratic processes. These units do not handle research methodology, which is instead managed by central methodology cores within research projects. These cores, focused on areas like bio sampling, epidemiology, and biostatistics, assist researchers in ensuring study quality, but this is separate from the tasks of the local coordination units.

Coordination Mechanism of Clinical Studies and Trials Funding during Future Infectious Disease Outbreaks

Outbreak Response Mechanism: what did and did not work in the PREPARE and RECOVER projects?

Herman Goossens - University of Antwerp, Belgium

Prof. Herman Goossens presents an analysis of the outbreak response mechanism developed and implemented within the PREPARE and RECOVER projects, focusing on what worked and what did not. He emphasizes the importance of linking outbreak funding mechanisms with response mechanisms to ensure effectiveness. PREPARE developed four modes: Mode 0 (interpandemic or peacetime), Mode 1 (limited threat), Mode 2 (potential threat), and Mode 3 (immediate threat), after two years of intense discussions and tabletop exercises. The response mechanism allowed quick decision-making by a small Outbreak Mode Committee, composed of key figures from various European institutions. This system was tested during various threats, including MERS, Ebola, chikungunya, and seasonal influenza, but was never escalated beyond Mode 1 until the COVID-19 pandemic in January 2020.

Goossens highlights that the PREPARE project allowed for a rapid response during the COVID-19 pandemic, moving from Mode 1 to Mode 2 and Mode 3 quickly despite the absence of immediate funding. The Outbreak Mode Committee activated the outbreak response even before the WHO had declared COVID-19 a public health emergency of immediate concern (PHEIC). However, the lack of funding delayed the initiation of clinical trials until March 2020. The experience revealed that while the mode system worked well, it failed to account for limitations within the European and global clinical research ecosystems.

Key hurdles included competition for research sites, a lack of research prioritization strategies, and the disconnection between public health and clinical research, which remains siloed. Additionally, Goossens notes that clinical research is not sufficiently integrated into practice across Europe, a factor contributing to the UK's more successful response.

Finally, Goossens stresses the need for better coordination between public funding criteria for clinical research and preparedness strategies. He advocates for an outbreak response mechanism with a more comprehensive and aligned approach involving multiple stakeholders, including (among others) European Commission services, ECDC, EMA, and national public health organizations.

Plenary discussion: towards a coordination mechanism of clinical studies and trials funding during infectious disease outbreaks

The aim of this plenary discussion is to explore the pathways towards a coordination mechanism of clinical studies and trials funding during infectious disease outbreaks. To guide the discussions, participants had been sent a number of pre-selected questions to reflect upon. Due to time constraints, however, not all questions could be addressed during the workshop.

> Question 1: Do you have suggestions on how to coordinate effectively and timely at the European level the funding of multinational clinical studies and trials during infectious disease outbreaks? What factors influence your preference(s)?
>
> Question 2: Which key elements should be considered and integrated in your organisation (and in your procedures) to facilitate at the European level the timely coordination of funding multinational clinical studies and trials during infectious disease outbreaks?
>
> Question 3: Which approaches do you propose for coordinating the monitoring and evaluation of clinical studies & trials being funded through a coordinated funding mechanism during infectious disease outbreaks? What are the main challenges?

On contracting and sponsorship aspects across national borders

Chris Butler (University of Oxford) highlights the significant challenges in managing contracting and sponsorship across national borders in international trials. He discusses the difficulties encountered during the PANORAMIC trial, where efforts to expand the trial to countries like the Republic of Ireland and the Netherlands were hindered by the absence of a legal mechanism to facilitate such expansion. Butler emphasizes the need for **streamlined agreements or mechanisms to enable smooth contracting, sponsorship, and data transfer across jurisdictions**, allowing different countries to recruit participants under the same protocol and into the same database.

Patrick Mallon (University College Dublin) proposes the concept of a "**sleeping protocol**" as a solution to contracting issues in multinational trials. He explains that having a pre-approved protocol and contract in place could significantly reduce the time required to resolve these issues when institutions first collaborate. Mallon suggests integrating this approach with the harmonization of pricing and data sharing mechanisms, which could have a substantial impact on the efficiency and effectiveness of future trials.

Herman Goossens (University of Antwerp) underscores the importance of **harmonizing ethical approvals**, citing ongoing discussions, such as those in the ACT-EU Priority 11 track 1, about establishing a single ethical committee for pandemic preparedness and response. He notes that these discussions are often emotionally charged due to the sensitivities surrounding member states' responsibilities. Goossens later emphasizes the need for strong leadership in developing consistent approaches to contracting, data sharing, and other critical aspects of multinational trials, lamenting the lack of decisive direction and the inefficiencies caused by fragmented efforts.

Inge Christoffer Olsen (EU-RESPONSE) explores an alternative model for conducting multinational trials, suggesting a **federated trial approach** where national trials adhere to a core protocol. While acknowledging that this approach has its challenges compared to a single sponsor structure, Olsen argues that it could facilitate faster implementation by allowing national trials to coordinate under a common framework. This model would require national funding bodies to align with a core protocol provided by an authoritative entity like the WHO or EU, potentially speeding up the process despite its limitations.

Frank Hulstaert (Belgian Healthcare Knowledge Center - KCE) discusses the pragmatic approach of pooling data after trials and suggests that the European Commission should **develop standardized templates for contracts** to avoid time-consuming negotiations when they are needed. He also shares an experience where a legal clause in a joint procurement contract prohibited research, causing significant delays in a vaccine trial in Belgium. Hulstaert stresses the importance of avoiding such clauses in future contracts to prevent similar setbacks.

Inesa Thomsen (UK Department of Health and Social Care) identifies the limitations of national funders in **moving money across borders** and suggests leveraging European Commission funding to address this issue. She points out that national funders are often restricted to spending within their own countries, but European funding could be used to compensate for under-recruitment in some sites by supporting over-recruitment in others, thus ensuring the necessary patient density for clinical trials.

Oonagh Ward (Health Research Board Ireland) discusses the **ongoing efforts by Era4Health** to establish a funding mechanism for multinational clinical trials. She explains that the initiative is looking at creating a central legal entity that would manage European funding and coordinate sponsorship responsibilities. National funders would support their respective country components of the trial, while the central entity would facilitate the cross-border movement of funds, addressing sponsorship issues and enhancing the overall efficiency of multinational trials.

On the need for political commitment

Herman Goossens (University of Antwerp) emphasizes the need to engage politicians in **understanding the importance of funding clinical studies and research**. He notes that while politicians often react to crises rather than prepare for them, it is crucial to convey the significance of clinical trials, especially in the context of preparedness. He also highlights the difficulty in getting politicians to prioritize research funding, as they may not be in office when the benefits of such preparedness become evident.

Chris Butler (University of Oxford) brings attention to the **World Health Assembly's resolution 75.8**, which focuses on strengthening clinical trials. He inquires about the extent to which colleagues are involved in implementing this resolution, which was passed at the ministerial level. This implies a need for ongoing collaboration and input from the health community to ensure effective implementation.

Herman Goossens follows up on the resolution, noting that he is part of the expert group working on this WHO guidance document that will soon be published. This document addresses various aspects of clinical trials, especially in low- and middle-income countries (LMICs) and aims to build a quality ecosystem for research. Goossens also emphasizes the need to **enhance the political relevance of clinical research at the EU level**, i.e. clinical research must be higher on the policy agenda. He reflects on past successes in raising the profile of antimicrobial resistance through European presidencies and suggests that upcoming presidencies should continue to push for clinical research to be prioritized.

Irja Lutsar (Tartu University) expresses concern about the increasing challenges in clinical research, particularly the **bureaucratic hurdles such as GDPR**, which discourage the younger generation from participating in clinical trials. She warns that if these issues are not addressed, clinical trials may move out of Europe, leading to a decline in European leadership in this field.

Ralf Heyder (NUM) agrees with the concerns about bureaucracy and regulatory red tape hindering clinical research. He suggests a dual strategy: **working with regulators** to improve the situation **and creating workarounds to reduce the administrative burden** on researchers. Heyder highlights the organizational challenge of ensuring that those directly involved in patient care are not overwhelmed by paperwork and advocates for more support systems to alleviate these challenges.

Concluding remarks and the way forward

Herman Goossens - University of Antwerp, Belgium

Em. Prof. Herman Goossens concludes by emphasizing the complexities and challenges in establishing a coordinated outbreak funding and response mechanism across Europe. He acknowledges that the initial ambitious plan for a tabletop exercise to test these mechanisms is unrealistic due to the need for further discussion on funding strategies and the development of an effective outbreak response mechanism. Goossens highlights the importance of developing a comprehensive vision for building sustainable, warm-based clinical trial networks in Europe.

He suggests that this vision should be integrated across different networks and disciplines, drawing inspiration from Australia's Clinical Trial Alliance.

Goossens stresses the necessity of strong leadership and top-down decision-making during pandemics. He emphasizes the importance of maintaining and expanding the database of national funders of clinical trial research, acknowledging the significant effort required to keep it up to date. Collaboration among national funders is crucial, and Goossens advocates for creating a sustainable platform for them to meet and address common issues, thereby building trust, which he identifies as essential for the success of any partnership. He also underscores the need for training programs to help funders gain experience in multinational clinical studies.

Finally, Goossens calls for urgent action to overcome the fragmentation of health research in Europe, warning that failure to do so would be a disservice to European citizens and compromise the EU's ability to tackle pandemic infectious diseases effectively. He sees this as a moral obligation and a critical opportunity to strengthen the EU's health research infrastructure, ultimately benefiting its citizens.