INNO4VAC

Innovations to accelerate vaccine development and manufacture

Workshop On Refining The Regulatory Context Of Controlled Human Infection Models

Inno4Vac CHIM models and issues encountered along the way

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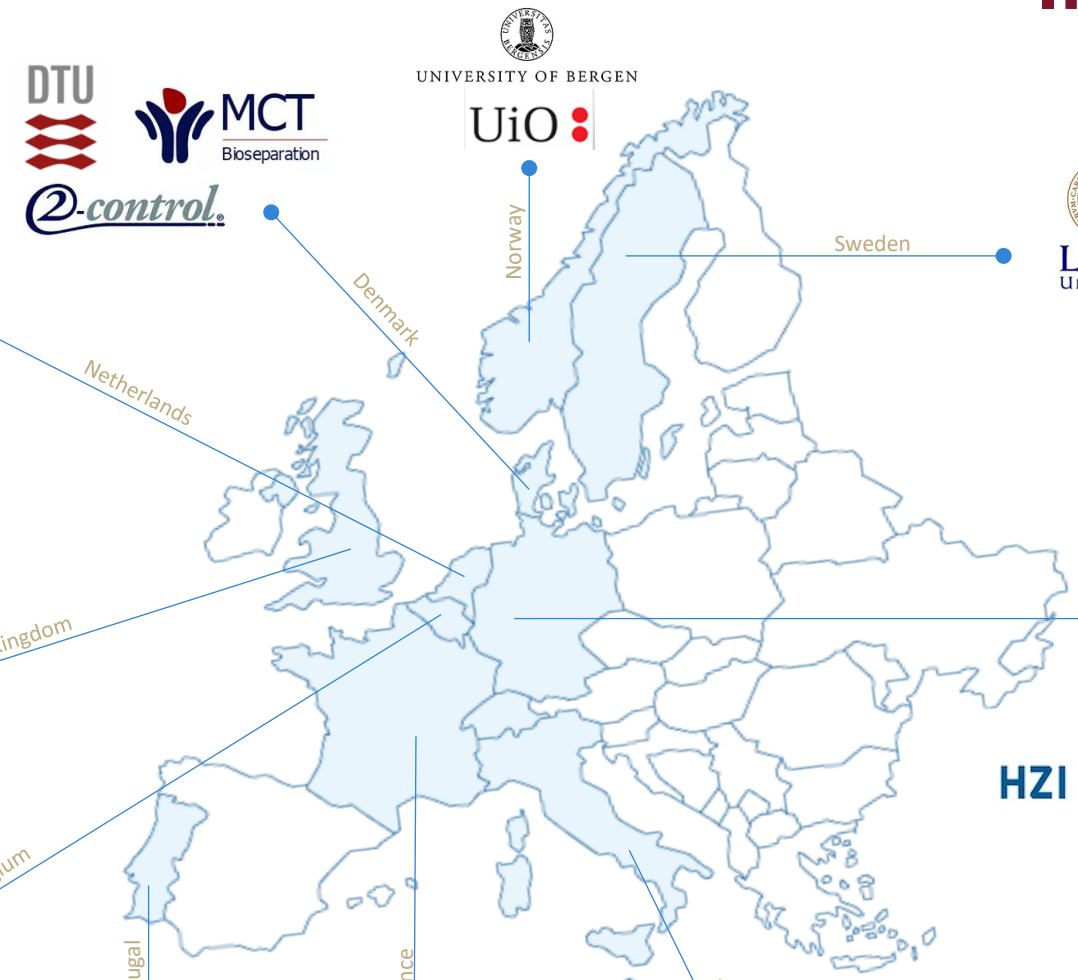
Inno4Vac partners

40 Partners from 11 countries



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Inno4Vac Strategy

Accelerate and de-risk development of new vaccines

MERMAID

ST3
Human *in vitro* Mucosa models and assays:

- *Development of mucosa models and assays prototypes (RESP, GI, UV)*
- *Case studies and validation of models*
- *Standardization, guidelines and roadmap*

CHIMICHURRI

ST2
Novel controlled human infection models:

C. difficile Influenza RSV

- *Development of new and improved CHIMs*
- *Positioning new developed CHIMs in regulatory framework*

ST1
Systems-immunology platform:

- *Open-access and cloud-based platform for in silico vaccine efficacy prediction*
- *Predictive algorithms of immune response generation after vaccination or infection*

VAXPRED

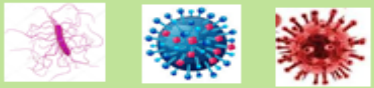
ST4
Mathematical modelling for Biomanufacturing:

- *Integrated platform for in silico vaccine manufacturing modelling*
- *Upstream and downstream processing models*
- *Stability prediction models*
- *Regulatory engagement*

VAXinS

Inno4Vac ST2 - CHIMICHURRI

ST2
Novel controlled human infection models:



C. difficile Influenza RSV

- *Development of new and improved CHIMs*
- *Positioning new developed CHIMs in regulatory framework*

Regulatory workshop on challenge strain development and GMP manufacture – A stakeholder meeting report

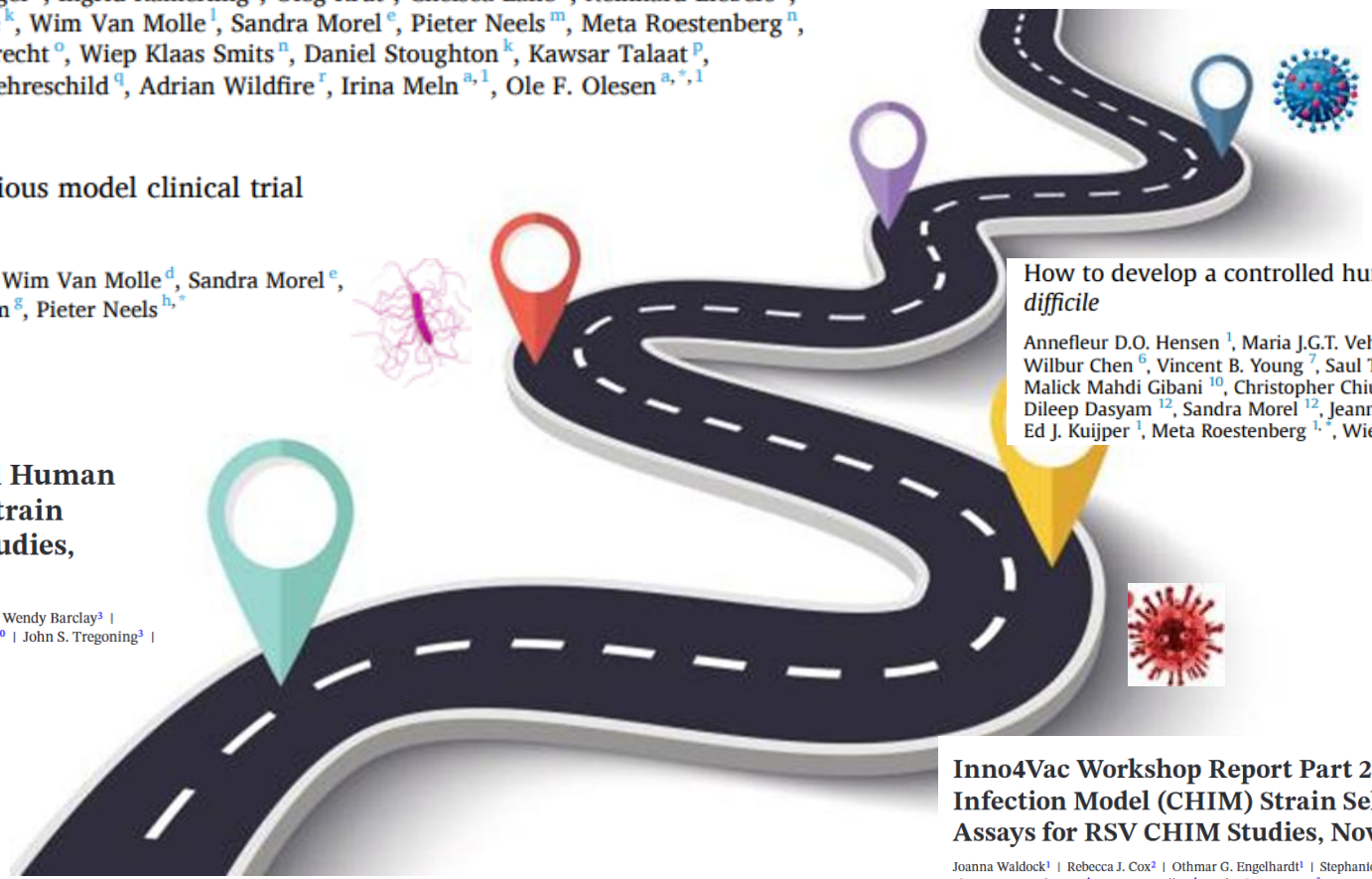
Nicoletta Corti [a], Christopher Chiu [b], Rebecca J. Cox [c], Clarisse Demont [d], Jeanne-Marie Devaster [e], Othmar G. Engelhardt [f], Andrew Gorringe [g], Khaole Hassan [e], Marcel Hoefnagel [h], Ingrid Kamerling [i], Oleg Krut [j], Chelsea Lane [k], Reinhard Liebers [a], Catherine Luke [k], Wim Van Molle [l], Sandra Morel [e], Pieter Neels [m], Meta Roestenberg [n], Michelle Rubbrecht [o], Wiep Klaas Smits [n], Daniel Stoughton [k], Kawsar Talaat [p], Maria J.G.T. Vehreschild [q], Adrian Wildfire [r], Irina Meln [a,1], Ole F. Olesen [a,*,1]

Regulatory workshop on standardisation of clinical procedures, endpoints and data robustness of human challenge studies – A stakeholder meeting report

Irina Meln [a,*,1], Victor Cnossen [b,1], Nicoletta Corti [a,1], Arno Andeweg [c], Marc Baay [d], Christopher Chiu [e], John Coia [f], Oliver Cornely [g,h], Rebecca J. Cox [i], Dileep Dasyam [j], Sigrid C.J. De Keersmaecker [k], Meagan Deming [l], Joanna Waldock [m], Othmar G. Engelhardt [m], Manman Guo [n], Okba Haj-Ali Saflo [j], Annefleur Hensen [o], Rienk Jeeninga [p], Simon Kolstoe [q], Oleg Krut [r], Ed J. Kuijper [o], Lorna Leal [c], Natalie Mazur [s], Kristin G.I. Mohn [t], Sandra Morel [j], Ab Osterhaus [t], Augustin Portela Moreira [u], Wiep Klaas Smits [o], Saranya Sridhar [v], Danny Toomey [w], Joop van Gerven [x], Maria J.G.T. Vehreschild [g,h], Juan Pablo Yarzabal [j], Paul Zimmer-Harwood [w], Pieter Neels [y,1], Ole F. Olesen [a,1], Meta Roestenberg [o,1], Ingrid M.C. Kamerling [b,o,1]

Ethical approval for controlled human infectious model clinical trial protocols – A workshop report

Euzebiusz Jamrozik [a,1], Katherine Littler [b,1], Irina Meln [c], Wim Van Molle [d], Sandra Morel [e], Ole F. Olesen [c], Michelle Rubbrecht [f], Shobana Balasingam [g], Pieter Neels [h,*]



How to develop a controlled human infection model for *Clostridioides difficile*

Annefleur D.O. Hensen [1], Maria J.G.T. Vehreschild [2,3], Dale N. Gerding [4], Oleg Krut [5], Wilbur Chen [6], Vincent B. Young [7], Saul Tzipori [8], Philipp Solbach [9], Malick Mahdi Gibani [10], Christopher Chiu [10], Sigrid C.J. de Keersmaecker [11], Dileep Dasyam [12], Sandra Morel [12], Jeanne-Marie Devaster [12], Nicoletta Corti [13], Ed J. Kuijper [1], Meta Roestenberg [1,*], Wiep Klaas Smits [1]

Inno4Vac Workshop Report Part 1: Controlled Human Influenza Virus Infection Model (CHIVIM) Strain Selection and Immune Assays for CHIVIM Studies, November 2021, MHRA, UK

Joanna Waldock[1] | Rebecca J. Cox[2] | Christopher Chiu[3] | Kanta Subbarao[4] | Adrian Wildfire[5] | Wendy Barclay[3] | Puck B. van Kasteren[6] | John McCauley[7] | Colin A. Russell[8] | Derek Smith[9] | Ryan S. Thwaites[10] | John S. Tregoning[3] | Othmar G. Engelhardt[1]

Inno4Vac Workshop Report Part 2: RSV-Controlled Human Infection Model (CHIM) Strain Selection and Immune Assays for RSV CHIM Studies, November 2021, MHRA, UK

Joanna Waldock[1] | Rebecca J. Cox[2] | Othmar G. Engelhardt[1] | Stephanie Ascough[3] | Albert Osterhaus[4] | Guus F. Rimmelzwaan[4] | Martin Ludlow[4] | John S. Tregoning[3] | Jacqueline U. McDonald[1] | Ursula J. Buchholz[5] | Rienk E. Jeeninga[6] | Charles. Sande[7,8] | Christopher Chiu[3]

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Selection of recommendations:

To RECs:

- Communication: foster ongoing discussions between REC's and researchers
- Review criteria: practical and flexible ethics criteria frameworks/checklists
- Third Party risk

To researchers:

- Tailor study application preparations
- Realise what REC's look for: explain study rationale, justification, participant selection
- Production and QC of challenge strains

Jamrozik et al. Biologicals 85 (2024)

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Guidance on strain selection

Recommendations on manufacturing requirements, including GMP-requirements: flexible adaptation based on GMP whilst taking (im)possibilities into account

Possibilities and liabilities of sharing strains

Corti N. et al. Biologicals 85 (2024)

Regulatory workshop on standardisation of clinical procedures, endpoints and data robustness of human challenge studies – A stakeholder meeting report

Irina Meln [a,*,1], Victor Cnossen [b,1], Nicoletta Corti [a,1], Arno Andeweg [c], Marc Baay [d], Christopher Chiu [e], John Coia [f], Oliver Cornely [g,h], Rebecca J. Cox [i], Dileep Dasyam [j], Sigrid C.J. De Keersmaecker [k], Meagan Deming [l], Joanna Waldock [m], Othmar G. Engelhardt [m], Manman Guo [n], Okba Haj-Ali Saflo [j], Annefleur Hensen [o], Rienk Jeeninga [p], Simon Kolstoe [q], Oleg Krut [r], Ed J. Kuijper [o], Lorna Leal [c], Natalie Mazur [s], Kristin G.I. Mohn [i], Sandra Morel [j], Ab Osterhaus [t], Augustin Portela Moreira [u], Wiep Klaas Smits [o], Saranya Sridhar [v], Danny Toomey [w], Joop van Gerven [x], Maria J.G.T. Vehreschild [g,h], Juan Pablo Yarzabal [j], Paul Zimmer-Harwood [w], Pieter Neels [y,1], Ole F. Olesen [a,1], Meta Roestenberg [o,1], Ingrid M.C. Kamerling [b,o,1]

Standardised immunological assays

Dose-escalation adaptive design

Recommendations on clinical and microbiological endpoints and their role in clinical development pathway

Meln I, Cnossen V et al. Biologicals 90 (2025)

Where are we on the road?

Where are we?

Clostridium difficile: 

LUMC: First cohort dosed, preparations for second cohort underway

RSV: 

CHDR: All participants dosed

Influenza: 

Strain selection performed, production underway, study planned for 2026

Issues encountered along the way

Clostridium difficile

Novel model developed

GMP-like production and development of the product dossier

Spread of spores: bystander risk?

RSV

Conducted as outpatient CHIM: what are the requirements?

Bystander risk? Burden to participants?

Influenza

Conducted as inpatient CHIM

Impact of quarantining on participants? What needs to be taken into account for participants? How to incorporate participant input in trial design?

General issues on the path

Adaptation to novel regulations (EU Clinical Trials Regulations)

Genetically Modified Organisms

Refinement of the regulatory context

Follow the recommendations of previous workshops: further advance dialogue with researchers, REC's and regulatory bodies

More paperwork not necessarily the solution, aim to improve the paperwork and incorporate flexibility

CHIMs are more and more needed and applied, need to continuously engage with regulatory bodies to keep up with all developments

Refine regulatory context of controlled human infection models in order to smoothly accelerate and de-risk vaccine development

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Thank you for your attention and we are looking forward to the discussion!

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