Conclusions & Recommendations

Conclusion of the meeting:

Controlled human infection models (CHIMs) can be helpful to study pathogenesis and for the development of vaccines (or anti-infective drugs). In CHIMs, human challenge agents are used to infect healthy volunteers, Therefore, ethical considerations include that the exposure studies need to be safe and results should be meaningful, e.g. contribute to better cure.

However, in some cases requirements of full GMP-based challenge agent production seem difficult to achieve and overly cumbersome.
This meeting informed us that, both in the US and in Europe, the level of GMP required is related to the phase of the study ('sliding scale GMP'), and, hence, is much more open to speedy drug development than anticipated.

Recommendations:

- The development of guidelines for human challenge agents on development and manufacture, ideally on World Health Organization (WHO) level.

- Guidelines are needed with a focus on strain selection, in particular with regard to strain infectivity (robust and reproducible attack rate), and strain characterization with regard to stability (retention of potency, genetics and phenotype) and purity (absence of adventitious agents).

- This should be done keeping in mind the actual relevance of the study (benefit/risk evaluation), the reproducibility (in other study sites), the transferability (to other regions/populations), and the specificity and the sensitivity of the individual CHIM.

- Towards strain characterization, Next Generation Sequencing (NGS) may be a valuable tool, but its use and limitations still need to be explored in this area. IABS-EU is organizing the 2nd Conference on Next Generation Sequencing for Adventitious Virus Detection in Human and Veterinary Biologics, November 13-14, 2019, in Ghent, see https://2nd-next-generation-sequencing-ghent-2019.iabs.org/ .

- Establish a reference repository of challenge agents, including methods for characterization and testing.

- When planning CHIMs or challenge agent development, seek early exchange with regulators to ensure acceptability of strain selection and manufacturing for later drug development.