Key issues:

- Due to the complexity of *in vivo* processes, alternative *in vitro* approaches such as cell culture or computer based systems cannot fully replace animal preclinical validation studies.
- Regulatory guidelines require proof of concept and safety studies performed in relevant animal models prior to testing promising vaccine candidates in clinical trials.
- Small animal models represent a cost- and time-efficient strategy to perform the screening, selection and prioritization of vaccine candidates, as well as often the only logistic viable alternative to antigen selection programs (*e.g.* reverse vaccinology).
- The use of rodent animal models allows identifying potential vaccine candidates, evaluating the most efficient vaccine formulation and defining the optimal route of delivery.
- The development of improved rodent animal models (*e.g.* humanized mice) is expected to facilitate translation of preclinical observations into the human system.
- The increase of ethical concerns requires an in-depth and broad education of the public to emphasize the necessity of animal research in order to develop efficient vaccines.
- Animal studies should be supported by emerging *in vitro* and *in silico* approaches, and ruled by the three Rs principles.