Objective
As technologically advanced high-throughput techniques are developed that replace, reduce or refine animal use, harmonization of validated protocols between international regulatory authorities is necessary to foster wide-reaching implementation. Because regulatory acceptance itself does not guarantee that an approved non-animal method will be adopted by manufacturers, interfacing with industry to disseminate information regarding exemptions from in vivo regulatory standards is necessary to confirm the preferential use of validated non-animal methods at the point of production. Here, we outline the process of bridging the gap between approval of non-animal vaccine batch potency testing by a regulatory body and the demonstrable implementation of those tests. We present our bridging paradigm, along with applications tailored to specific vaccine scenarios, in order to demonstrate a successful strategy that increases the use of available non-animal potency testing methods.

Methods
This bridging paradigm can be visualized as an information collection and dissemination matrix that is customized to the needs of each vaccine for which a non-animal potency test exists.

PETA's bridging paradigm can be applied and customized according to the information available for a given non-animal potency testing method. PETA has initiated this process for each of the vaccines in discussion at this workshop, as summarized below. For each vaccine, information collection and confirmation of regulatory use are necessary prerequisites for identifying essential next steps in the process. In some cases, the process of promoting implementation of a non-animal method identifies instances of possible non-compliance with the Animal Welfare Act or other regulations. In all cases, validation data and SOPs or SAPs for non-animal methods are shared with regulators and manufacturers, followed by efforts to confirm acceptance and implementation by manufacturers.

Methods in application

PETA's bridging paradigm can be applied and customized according to the information available for a given non-animal potency testing method. PETA has initiated this process for each of the vaccines in discussion at this workshop, as summarized below. For each vaccine, information collection and confirmation of regulatory use are necessary prerequisites for identifying essential next steps in the process. In some cases, the process of promoting implementation of a non-animal method identifies instances of possible non-compliance with the Animal Welfare Act or other regulations. In all cases, validation data and SOPs or SAPs for non-animal methods are shared with regulators and manufacturers, followed by efforts to confirm acceptance and implementation by manufacturers.

Case studies
Ensuring that implementation becomes a reality following validation of non-animal methods requires steps beyond the validation of methods and their implementation at one manufacturer and possible AWA violations (e.g., USDA/FDA?—). This process has successfully involved eliminating barriers to exemptions from section 113.67 for veterinary vaccines. In the European Union, this process is being applied to advancing the implementation of non-animal potency tests for pertussis and tetanus vaccines.

This procedure establishes the acceptability of data from novel methods by regulatory authorities and disseminates information on available and accepted non-animal approaches via stakeholder alerts, involves the press in publicizing accepted non-animal techniques, and informs manufacturers on implementation of these methods. By engaging with regulators and manufacturers, PETA has effectively promoted 3R approaches to vaccine batch potency testing. Despite a lack of transparency in the process of non-animal test method approval in the US, we have shown that petitioning for regulatory acceptance of internationally validated methods can hasten the approval of non-animal testing methods and, conversely, the removal of obstacles in said method in a way that demonstrates what the US authorities, PETA has successfully promoted 3R approaches to vaccine batch potency testing. Despite a lack of transparency in the process of non-animal test method approval in the US, we have shown that petitioning for regulatory acceptance of internationally validated methods can hasten the approval of non-animal testing methods and, conversely, the removal of obstacles in said method in a way that demonstrates what the US authorities, PETA has successfully promoted 3R approaches to vaccine batch potency testing. Despite a lack of transparency in the process of non-animal test method approval in the US, we have shown that petitioning for regulatory acceptance of internationally validated methods can hasten the approval of non-animal testing methods and, conversely, the removal of obstacles in said method in a way that demonstrates what the US authorities, PETA has successfully promoted 3R approaches to vaccine batch potency testing. Despite a lack of transparency in the process of non-animal test method approval in the US, we have shown that petitioning for regulatory acceptance of internationally validated methods can hasten the approval of non-animal testing methods and, conversely, the removal of obstacles in said method in a way that demonstrates what the US authorities, PETA has successfully promoted 3R approaches to vaccine batch potency testing. Despite a lack of transparency in the process of non-animal test method approval in the US, we have shown that petitioning for regulatory acceptance of internationally validated methods can hasten the approval of non-animal testing methods and, conversely, the removal of obstacles in said method in a way that demonstrates what the US authorities, PETA has successfully promoted 3R approaches to vaccine batch potency testing. Despite a lack of transparency in the process of non-animal test method approval in the US, we have shown that petitioning for regulatory acceptance of internationally validated methods can hasten the approval of non-animal testing methods and, conversely, the removal of obstacles in said method in a way that demonstrates what the US authorities, PETA has successfully promoted 3R approaches to vaccine batch potency testing. Despite a lack of transparency in the process of non-animal test method approval in the US, we have shown that petitioning for regulatory acceptance of internationally validated methods can hasten the approval of non-animal testing methods and, conversely, the removal of obstacles in said method in a way that demonstrates what the US authorities, PETA has successfully promoted 3R approaches to vaccine batch potency testing.