**IMPLEMENTATION OF THE THREE RS IN CANADIAN VACCINE QUALITY CONTROL TESTING: OBSTACLES AND OPPORTUNITIES**

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**BACKGROUND**

- Vaccines must undergo extensive quality control testing for safety and potency before they are released onto the market.
- Testing typically requires large numbers of animals, often involves substantial pain and distress, and may have death as an endpoint (Council of Europe, 2008; Hendriksen, 2002).
- Alternative testing methods exist which have not yet been accepted into Canadian regulation.

**CASE STUDY**

We are conducting a case study to obtain the perspectives of various stakeholders on obstacles and opportunities to implementing the Three Rs in vaccine quality control testing. Understanding these factors should facilitate the adoption of scientifically sound alternative methods into Canadian vaccine testing.

**Participants**

- Participants for the study are being selected through purposive sampling and snowball sampling (Palys & Atchison, 2007).
- These preliminary results are based on responses from four participants: two government regulators and two industry scientists.

**Methodology**

- Perspectives are being collected through in-depth, semi-structured interviews.
- Interviews are based on twelve open-ended questions.
- All interviews are audio recorded and conducted under strict anonymity.

**PRELIMINARY RESULTS**

**Opportunities**

- **Variability of Animal Tests**
  A motivator for both industry and regulators to replace the histamine sensitivity assay, as varying results have led to false positives.

- **Vaccine Complexity**
  *In vitro* assays are particularly useful for combination vaccines as they can be tailored to detect specific residues.

- **Reduction in Animal Use**
  Both industry and regulators expressed interest in reducing the use of animals in vaccine testing for ethical reasons.
  Industry aims to use fewer animals to save resources, manpower and time.

- **International Harmonization**
  Industry has spearheaded harmonization efforts with international agencies to implement alternative methods.

- **Publication in Pharmacopoeia**
  The publication of alternative methods in pharmacopoeia gives Canadian regulators more confidence to accept a new test.

**Obstacles**

- **Protection of Vulnerable Individuals**
  Both regulators and industry are highly motivated to ensure that vaccines are effective and safe as they are given to infants and children.

- **Variability of Animal Tests**
  *In vitro* method validation is difficult due to lack of correlation between *in vivo* and *in vitro* results.

- **Biological Relevance**
  ELISAs for potency testing measure antibody titer, not whether these antibodies neutralize the disease toxin or antigen (*N.B. this is not the case with the D/T serological assay, which has been shown to detect neutralizing antibodies*).

- **Market Requirements**
  Manufacturers must comply with a country’s regulations and employ an animal method if requested.

The factors listed here were selected due to their high frequency of response.

**GOING FORWARD**

The preliminary results suggest that industry and the Canadian government are open to implementing the Three Rs for vaccine quality control testing, but that the methods adopted must be proven to be reliable and biologically relevant. Further harmonization across countries would assist in alternative method implementation.

The authors wish to thank all of the people who have participated in this study, as well as Emily Verlinden for her considerable assistance in the preparation of this poster.

This study received ethical review and approval from IRB services.

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