International Proficiency Study of the Single Radial Immuno Diffusion Test (SRID) for Influenza Vaccine Manufacturers and Regulators from Developing Countries

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Study Objective

- Performance of an international laboratory proficiency study for vaccine manufacturers and national vaccine regulators from selected developing countries with the aim to assess the effectiveness of hands-on WHO training workshops carried out under the umbrella of GAP in the field of quality control for inactivated seasonal influenza vaccines since 2008
Historical Background

- Since 2007, in collaboration with international donors, the WHO has been providing grants for developing country manufacturers in support of the establishment of domestic influenza vaccine production in their countries.

- Through the involvement of numerous partners, the grants are complemented with concrete technical support, including bench level hands-on trainings, offered not only to manufacturers but their domestic NRA/NCLs which ultimately are responsible for market authorization and continuous regulation thereafter.
Why SRID?

- Since the late 1970's SRID is the standardized test which used to quantitate the potency of inactivated influenza vaccines.

- It became, and still is, the key lot release test which is performed by both manufacturers and regulators.

- The test was also identified as the key release test by WHO and included in the curriculum of trainings offered in the area of quality control.
Background

- From 2008 onward targeted WHO training workshops were organized and founded to provide hands-on training for the key lot release tests at the National Institute of Biological Standards and Control (NIBSC), and at the former National Vaccine Institute (NVI) of the Netherlands, for both grantees and their NRA/NCLs, which have the mandate to licence and regulate these newly developed vaccines.

- The theory and practice of SRID testing was the most focused on activity at these courses.
The WHO-CBER Collaborative Agreement

- In 2012 in support of the GAP initiative a special 5 years cooperative agreement was established with the US FDA/CBER

- The aim of the cooperative agreement is to strengthen the capacity of developing country NRA/NCLs to regulate vaccines with emphasis and focus on influenza

- In the last few years numerous NIBSC courses took place in the area of quality control for influenza vaccines which we organized mainly for grantee country vaccine regulators
The proposed proficiency study will provide an objective, internationally comparable measurement tool to assess the effectiveness of the numerous WHO founded SRID trainings carried out during the last half decade.

The result of the proficiency study will also reflect on how was the SRID test introduced and implemented at the national level in the grant recipient countries.
From the APW between WHO and NIBSC

- ".....Administrative organization and confirmation of lists of NRA/NCL and manufacturer participants will be carried out by WHO following invitations for participation in the study....."

- ......Up to twenty two manufacturers and/or NLCs selected across the five WHO regions participating in the influenza vaccine production capacity building programme (GAP) are targeted to participate in the study....."
Where are we now?

- 2012: signature of the cooperative agreement with a work plan under Objective 4 for quality control training courses at NIBSC and the international SRID proficiency study thereafter

- 2012-2013: Hands-on courses were taking place at the NIBSC HQ in Potters Bar, England

- 2013-2014: First announcement of the proficiency study plan at the 6th Partners' Meeting in Dubai, UAE. Development (NIBSC and WHO) and approval (sponsor) of the Study Protocol

- 2015: Securing study antigen from IFPMA ("Engagement of IFPMA IVT with NIBSC to supply inactivated influenza vaccine for SRID proficiency study in developing countries"), preparation of reference antigens and reference sera for the tests
Next steps

- Distributions of test antigens, reagents and study protocol to participants
- Performing the tests (three times) at participants' and NIBSC laboratories
- Submitting study results to NIBSC for analysis
- Draft report to be submitted to WHO
- Report made available to participants, presentations at international meeting(s), and, pending on study outcome, publication in a peer reviewed journal
Outline of Study Protocol-1

- Details on types and number of samples to be obtained from manufacturers: three blinded samples of regular inactivated trivalent seasonal influenza vaccine

- Tests to be undertaken on candidate materials before shipping to participants (screening). NIBSC performs potency tests of study vaccine to confirm that it fits for the study

- Proposed SRID test protocol: it is suggested that participants use the WHO/NIBSC adapted procedure, however, local procedures may also be used
Outline of Study Protocol-2

- Types and numbers of samples to be distributed to each participant: sufficient numbers of vaccine lots, SRID antigen and antiserum reagents will be supplied.

- For example: if a laboratory selects to use the NIBSC protocol as their assay choice for the study, they would receive six ampoules of antigen and three ampoules of antiserum reagent for each vaccine strain; and six samples of each vaccine lot.

- Laboratories will be supplied with the ‘instructions for use’ for all reagents, namely reference antigen and antiserum reagents for the three components of the test vaccine.
Typically, seasonal influenza vaccines are supplied as a trivalent vaccine, containing H1N1, H3N2 and B influenza virus strains. The content of each of these strains is estimated using homologous antigen and antiserum potency reagents.

NIBSC antigen reagents for the study were prepared from an inactivated, partially purified whole virus preparation which is then freeze dried. A potency value in µg HA/mL is assigned according to the results of an international collaborative study periodically performed.
Outline of Study Protocol: Reagent preparation-2

- These reagents are single use, reconstituted in distilled water and used as reference preparations in the SRID vaccine potency assay.

- NIBSC antiserum reagents are prepared from sheep serum. Animals were immunised through using specifically treated (bromelain cleaved) HA of an influenza virus.

- These reagents contain preservative and will be supplied as liquid preparations for use. It is provided to participants in conjunction with the appropriate test antigens.
Outline of Study Protocol: Instruction to participants

- A minimum of three separate assays to be performed, as elaborated in the NIBSC protocol, or alternatively the participant’s own SRID protocol.

- Raw data, zone sizes, to be entered on forms provided by NIBSC

- Calculated potency values are forwarded by participants for analysis to NIBSC

- Participants will also be asked to record any deviations from the protocol they used.
Outline of Study Protocol: Data analysis and Study Report

- Data will be analysed by NIBSC as described in the study protocol
- An anonymised report will be generated.
- Participants will be supplied with their individual participant code number
- Draft report is prepared for WHO input and approval (planned for autumn of 2015)
- Presentation to stakeholders at meeting(s), publication (2016)
Thank you!