Switching from in vivo to in vitro potency: 2 case studies for setting new potency acceptance criteria

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Sanofi rabies vaccine portfolio is constituted of 2 commercialized vaccines (IMOVAXRABIES and VERORAB™) and one new vaccine under development (VRVg) aimed at replacing both current commercialized vaccines worldwide in mid-term.

The current Rabies vaccine potency is the NIH *in vivo* test. This mouse intracranial challenge test is variable and time consuming. In the context of the VRVg vaccine development, Sanofi initiated the development and validation of a Rabies G protein ELISA to facilitate production process development and optimization and to replace the *in vivo* NIH potency test on the final product.

In this presentation are presented the 2 approaches used to support the introduction of Rabies G protein ELISA test as potency test on both the new VRVg rabies vaccine and the commercialized VERORAB™ rabies vaccine.

For both vaccines, the use of Rabies G protein ELISA as surrogate of potency on final product is supported by a significant data package demonstrating the suitability of the Rabies G protein ELISA, which includes: mAbs characterization, ICH validation package, capability to detect G protein alteration and higher discriminating power of the Rabies G protein ELISA for the detection of subpotent lots in comparison to the NIH test.

The Rabies G protein ELISA has been developed for VRVg process and product development. Rabies G protein ELISA supports drug substance process monitoring and is done in parallel with NIH test on clinical batches. The strategy is to submit in the VRVg CTD, G protein ELISA as potency assay with acceptance limits both for release and stability supported by clinical data. In a second step to define in-house action limits based on historical to follow manufacturing process consistency.

For the VERORAB™ Vaccine, the implementation of Rabies G protein ELISA on final product is associated with the definition of release and stability ELISA acceptance limits based on manufacturing process consistency calculated on G protein ELISA results from 279 VERORAB™ lots. In addition, the Rabies G protein ELISA has been implemented for drug product formulation and for drug substance monitoring.