Experience with EUL During ERVEBO® Submission

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Background

- The second largest outbreak of the Ebola virus disease was occurring at the time the Merck vaccine was being registered and WHO prequalified.
- That led to challenges as a result of the need to supply the investigational vaccine for use in the outbreak while simultaneously qualifying the manufacturing processes and supporting regulatory activities.
- WHO defined an Emergency Use Assessment and Listing Procedure in response to the 2014-2016 Ebola outbreak to define the steps that WHO will follow to establish the:
  - eligibility of products
  - minimum information required
  - assessment to make a product available under a limited time listing status, while further data is being gathered and evaluated
- It is intended for use primarily for public health emergencies of international concern

EUL Experience

- Merck submitted documentation to support WHO Emergency Use Listing (EUL) of ERVEBO® prior to conditional marketing authorization, WHO prequalification and African NRA approval, however, the vaccine was not ultimately listed
- The vaccine was provided to at risk subjects and healthcare providers through other means
- Highlights
  - The EUL process assumes that emergency regulations (EUA) are in place in the country in which the vaccine will be used
  - Those countries which do have EUA are not harmonized
  - It works best for products that are licensed in the country of origin

Lessons Learned

- Emergency regulations did not exist in the countries most impacted by the Ebola virus disease. This and deployment concerns prevented the listing of the vaccine.
- For an unlicensed product, use outside of a clinical protocol requires careful consideration of many aspects, including
  - liability coverage
  - export from the country of origin to the country of use
  - the need to draft package inserts for an investigational product
  - traceability for use and mechanisms to collect safety data
- Enabling early use is its own, discrete, complex, regulated body of work, which requires full time planning and attention (with focus on regulatory pathways)
- The quantity of a developmental vaccine to support clinical trials is much less than needed to curb an outbreak, so vaccine supply should be considered carefully

Conclusion

- Since that time, WHO has updated the EUL guideline based on the issues seen in the ERVEBO® EUL process

  https://www.who.int/diagnostics_laboratory/eual/procedure/en/#:~:text=The%20EUAL%20is%20a%20risk,public%20health%20emergencies%20if%20appropriate.

- WHO is working with global NRAs to align more closely the EUA processes within countries or to have them accept the EUL from WHO to allow Covid-19 vaccine use in their countries.