

TITLE: PREPAREDNESS AGAINST PANDEMIC INFLUENZA: PRODUCTION OF AN OIL-IN-WATER EMULSION ADJUVANT IN BRAZIL

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ABSTRACT

Influenza pandemics are unpredictable but recurring events that can have severe consequences on worldwide human health. Advanced planning and preparedness are critical to mitigate the impact of a global pandemic. Increasing pandemic influenza vaccine manufacturing capacity is considered strategic by WHO. Antigen sparing by employing adjuvants also represents a key technology for global pandemic influenza preparedness. Moreover, during a pandemic, adjuvants are particularly beneficial for influenza vaccines where a rapid response is required or there is a need to improve the overall immune responses, especially in patients with impaired immunological responses such as the pediatric and elderly populations. We describe here the development of an oil-in-water adjuvant emulsion, named IB160, to be combined with pandemic influenza antigens as preparedness for pandemic influenza. We have focused on the production and stability studies and the immune response of the H7N9 vaccine combined with IB160. H7N9 influenza is considered a potential pandemic influenza virus and the H7N9 vaccine was considered a model to evaluate the adjuvant effect of IB160 oil-in-water emulsion. The average results from 10 consistency lots of IB160 produced under GMP conditions were: pH 6.4 ± 0.05 ; squalene 48.8 ± 0.03 mg/ml; osmolality 47.6 ± 6.9 mmol/kg; Z-average 157157 ± 2 nm, polydispersity index (PDI) of 0.085 ± 0.024 and endotoxin levels < 0.5 EU/mL. The emulsion particle size was stable for at least six months at 25°C and 24 months at 4-8°C. Two doses of H7N9 vaccine formulated at 7.5 µg/dose or 15 µg/dose with adjuvant IB160 showed a significant increase of HAI and seroconversion when compared to controls. Thus the antigen-sparing capacity of IB160 can potentially increase the production of the pandemic vaccine and represents an important achievement for preparedness against pandemic influenza in Brazil and globally and may also be useful as vaccine adjuvant for other non-influenza vaccine formulations. Currently, H7N9 vaccine combined with IB160 is under phase I clinical trial.

KEYWORDS: adjuvant, vaccine, pandemic flu, influenza vaccine.

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