**Summary of WHO position on use of fractional doses of Yellow fever vaccine, June 2017**

This WHO position on the use of fractional doses of Yellow fever vaccine (YF), published in June 2017, is an addendum to the corresponding vaccine position paper for vaccines and vaccination against yellow fever published in July 2013. It addresses the potential use of fractional dose YF (fYF) vaccine in the context of emergency supply shortages. The recommendations from the 2013 position paper regarding standard YF vaccination remain the same.

**Background**

In 2016, large YF outbreaks throughout central Africa exhausted the global vaccine stockpile while large populations remained at-risk. As an exceptional measure, the use of fYF vaccination was considered. The theoretical basis for such an approach is that the minimum potency recommended by WHO for use in humans should not be less than 1000 international units (IU)/dose, while the potency at release of YF vaccine standard doses is frequently many-fold higher.

Few studies have assessed the safety and immunogenicity of fYF vaccine. Of most relevance is a study of one YF vaccine tested at 6 potencies administered subcutaneously: the full potency at release of 27 476 IU, as well as dilutions of 10 447 IU, 3 013 IU, 587 IU, 158 IU, and 31 IU in a study population of 749 adult males. At 30 days post-vaccination, seroconversion rates were high (97%–99%) for vaccine doses of 587 IU and higher. Among those who originally seroconverted, >97% still had detectable antibodies ~10 months post-vaccination in all vaccine potency categories except the lowest (31 IU).

Based on these data, as an exceptional measure, fYF vaccination was used in Kinshasa, Democratic Republic of the Congo in August, 2016. A total of 7.9 million individuals >2 years of age were administered 1/5 of the standard YF vaccine dose, while pregnant women and children < 2 years of age received the full dose. No safety signals associated with fYF vaccination were detected. An observational study conducted during the Kinshasa campaign found 98% seroconversion at 28 days for the study participants given fYF. However, important research questions remain, including the duration of immunity with fYF and its use in special populations.

**WHO Position**

Recent outbreaks have highlighted the critical importance of strong routine YF immunization programmes and mass vaccination campaigns in line with the WHO EYE Strategy for the prevention of YF outbreaks.

A fractional YF vaccine dose can be used as part of an emergency response to an outbreak if there is a shortage of full-dose YF vaccine that exceeds the capacity of the global stockpile. This is not intended to serve as a longer-term strategy or to replace established routine immunization practices. As soon as the YF vaccine supply situation can meet the immediate need, the use of fYF vaccination should be replaced by standard full-dose YF vaccination.

Based on the available clinical data, the minimum dose administered should preferentially contain 3000 IU/dose, but no less than 1000 IU/dose, and the minimum volume of the dose should
not be less than 0.1 mL because of the practical difficulties of delivering dose volumes smaller than this. Determining the most suitable volume (i.e. 1/2 or 1/5 of a standard dose) to be used as a fractional dose should be done by the country, taking into consideration the available vaccine product and its release specifications. Until long-term protection is better documented, YF vaccination does not meet YF vaccination requirements under the International Health Regulations (IHR), and proof of vaccination for international travel currently requires re-vaccination with a standard full dose.

There are important research gaps that need to be addressed to facilitate flexibility in the use of fractional doses during YF vaccine shortages. Taking a short-term and pragmatic approach, non-inferiority immunogenicity studies of all 4 WHO prequalified YF vaccines are needed, as well as non-inferiority immunogenicity studies in special populations with consideration of ethnicity, age, and prior flavivirus exposure. Of particular importance, given the consequences for international travel involving IHR requirements, is the confirmation of long-term protection with fractional dosing, including the potential need for revaccination.