Summary of JCVI consideration of the number of doses of influenza vaccine for influenza vaccine-naïve children
March-April 2013

UK health departments asked JCVI for advice on the number of doses of influenza vaccine offered to influenza vaccine-naïve children when extending the routine influenza immunisation programme to children. This advice was being sought to inform planning and vaccine procurement decisions for extending the routine programme. Current guidance[1] and vaccine manufacturers' Summaries of Product Characteristics indicate that influenza vaccine-naïve children aged six months to less than nine years should be offered two doses of influenza vaccine with at least four weeks between the first and second dose.

JCVI considered by correspondence evidence from clinical trials on the effectiveness of one and two dose schedules of live attenuated influenza vaccine (LAIV) in influenza vaccine-naïve young children[2,3,4,5]. In addition, the committee considered an analysis of the difference in the population health impact and the cost effectiveness of one and two dose schedules of LAIV for influenza vaccine-naïve children aged up to nine years when extending the programme to all pre-school children from two years of age and primary school-aged children and an analysis of the direct health impact only of either two doses of LAIV to two year old children or one dose to two and three year old children. These analyses were based on a mathematical modelling study reviewed previously by the committee[6,7,8,9].

JCVI noted that data from clinical trials suggest that a second dose of LAIV provides modest additional protection against influenza infection (e.g. 60% versus 77% vaccine effectiveness for one and two doses, respectively[5]) and that a single dose of LAIV may provide similar protection to children as two doses of inactivated influenza vaccine[5,10]. Whilst an analysis of the population impact of one and two dose schedules of LAIV when extending the immunisation programme to all pre-school

[1] Influenza chapter (2012/13 influenza season version). Immunisation against infectious disease ('the Green Book').
[2] Belshe *et al.* (1998) The efficacy of live attenuated, cold-adapted, trivalent, intranasal influenzavirus vaccine in children. *N Eng J Med.* 338, 1405-1412.
[3] Bracco Neto *et al.* (2009) Efficacy and Safety of 1 and 2 doses of live attenuated influenza vaccine in vaccine-naïve children. *Pediatr Infect Dis J.* 28, 365-371.
[4] Block *et al.* (2009) Efficacy of a single dose of live attenuated influenza vaccine in previously unvaccinated children: a post hoc analysis of three studies of children aged 2 to 6 years. *Clin Ther.* 31, 2140-2147.
[5] Rhorer *et al.* (2009) Efficacy of live attenuated influenza vaccine in children: a meta-analysis of nine randomized clinical trials. *Vaccine.* 27, 1101-1110.
[6] Cromer *et al.* Estimating the burden of influenza by risk group. *Unpublished.*
[7] Baguelin *et al.* Reconstructing past influenza epidemics from consultation, virological surveillance data and a contact survey. *Unpublished.*
[8] Baguelin *et al.* The cost effectiveness of vaccination against seasonal influenza in England. *Unpublished.*
[9] JCVI statement on the annual influenza vaccination programme – extension of the programme to children. 25 July 2012
[10] Jefferson *et al.* (2012) Vaccines for preventing influenza in healthy children. *Cochrane database of Systematic Reviews.* Issue 8, Art. No. CD004879.

children from two years of age and primary school-aged children, as is planned from 2014, suggests that a two dose schedule would prevent more infections, hospitalisations and deaths across the whole population (assuming high compliance with a two dose schedule), set alongside the additional costs it may be of borderline cost effectiveness. However the results of this analysis are highly uncertain as a large majority of the benefits of the programme, including the additional benefits of a second dose, rely on indirect protection of unvaccinated individuals by reducing transmission from those vaccinated. The additional population impact of the second dose may be overestimated if a single dose of LAIV leads to a greater reduction in the infectiousness of vaccinated children than predicted from vaccine effectiveness against clinical disease. No data were considered on the cost effectiveness of a smaller extension to the programme as is planned for 2013. However, an analysis of the direct impact of either two doses of LAIV to two year old children or one dose to two and three year old children (i.e. in the absence of wider vaccination of children beyond three years of age when any indirect protection that would accrue would be expected to be very limited) suggests that the greater health impact would be obtained if the available quantity of vaccine was provided through a one dose schedule to the larger number of children.

Although specific data are lacking, JCVI also considered that a two dose schedule is likely to make the extended programme appreciably more complex and challenging to implement, particularly in the school setting but possibly less so for general practice. Compliance with the two dose schedule in either setting may be poor[11].

JCVI concluded, therefore, that when extending the routine programme to children from 2013, a single dose of LAIV should be offered to children irrespective of whether influenza vaccine had been received before or not. However, influenza-vaccine naïve children who are aged six months to less than nine years in clinical risk groups, or who are offered inactivated influenza vaccine as LAIV is unsuitable for them, may have greater benefit from the direct protection provided by a second dose of vaccine. Ensuring that the offer of a second dose of vaccine is effectively and uniformly offered to these individuals may be challenging, particularly in school or mixed school-GP delivery models, but JCVI considers that this offer should continue to be made when extending the routine programme.

[11] Jackson *et al.* (2006) Compliance with the recommendations for 2 doses of trivalent inactivated influenza vaccine in children less than 9 years of age receiving influenza vaccine for the first time: a Vaccine Safety Datalink study. *Pediatrics.* 118, 2032-2037.