DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

DATE	**March 23, 2015**
FROM	**LCDR Matthew Steele, PhD**
THROUGH	**Loris McVittie, PhD**
STN	**125525/0**
PRODUCT	**Diphtheria and Tetanus Toxoids and Acellular Pertussis Adsorbed and Inactivated Poliovirus Vaccine**
APPLICANT	**Sanofi-Pasteur Ltd**
SUMMARY	**Review of the Applicant's cross-reference strategy** **Review of Expiration date**

Background:
On March 24, 2014 the Applicant, Sanofi-Pasteur Ltd, submitted a Biologics License Application for a tetravalent vaccine, Diphtheria and Tetanus Toxoids and Acellular Pertussis Adsorbed and Inactivated Poliovirus Vaccine (DTaP-IPV). The applicant proposed QUADRACEL as the trade name. The proposed indication is prevention of diphtheria, tetanus, pertussis and poliomyelitis in children ages 4 through 6. It is intended as a 5th dose booster in children who received Pentacel (consisting of DTaP, IPV and Haemophilus influenza type B [HiB] antigens) and/or Daptacel previously.

Since Quadracel is comprised of the liquid DTaP-IPV formulation used to reconstitute the HiB component for Pentacel, the applicant incorporated by cross-reference the manufacturing information for Quadracel from their approved Pentacel vaccine BLA (STN 125145).

STN 125525/0.4

On May 13, and May 20, two Information Requests (IR) were sent to the applicant asking for clarification of the extent of the cross-reference of their Pentacel BLA (STN 125145) since there have been a number of supplements submitted and either approved or pending since the original licensure of Pentacel The applicant responded in STN 125525/0.4 on November 13, 2014. CBER accepted this response, which explained that the original Pentacel BLA and all approved supplements are covered in the cross-reference, with any pending supplements not under consideration for the original approval of Quadracel. Additionally, the applicant proposed, and CBER agreed, that future trans-BLA supplements which pertain to both Pentacel and Quadracel would have the information to be reviewed submitted under the Pentacel BLA.

Expiration dating period of the Final Drug Product

I reviewed the Pentacel supplement 125145/200 in which CBER concurred with the Applicant's request to extend the expiration date for the DTaP-IPV component to 36 months. Since the manufacture of Quadracel is identical to the DTaP-IPV component of Pentacel, the expiration date of the Quadracel product will also be identical. This date runs from the date of final formulation of the final bulk product, which can occur up to (b) (4) prior to final filling. Therefore, the expiration date of the final Quadracel product will be 36 months from the time of formulation of the final drug product.