



EUROPEAN MEDICINES AGENCY  
SCIENCE MEDICINES HEALTH

22 October 2015  
EMA/CHMP/657099/2015  
Procedure Management and Committees Support Division

## Assessment report for paediatric studies submitted according to Article 46 of the Regulation (EC) No 1901/2006

### **Fluenz Tetra**

INFLUENZA VACCINE (LIVE ATTENUATED, NASAL)

Procedure no: EMEA/H/C/002617/P46/009

### **Note**

Assessment report as adopted by the CHMP with all information of a commercially confidential nature deleted.



# Rapporteur's Assessment Report for the Post- Authorisation Measure number P46 009

## **Fluenz Tetra**

International non-proprietary name: Influenza vaccine (live attenuated, nasal)

Procedure No. EMEA/H/C/2617/P46 009

Marketing authorisation holder: Medimmune

Date of this report:	24/09/2015
Deadline for comments:	12/10/2015

## Administrative information

Name of the Rapporteur	<b>Name : Daniel Brasseur</b> Email: daniel.brasseur@ext.emea.europa.eu
Rapporteur contact person:	<b>Name : Annick Dujardin</b> Email: annick.dujardin@afmps.be
Names of the Rapporteur's assessors	<b>Name : Francoise Guillaume</b> Email: francoise.wuillaume@fagg-afmps.be <b>Name : Nele Berthels</b> Email: nele.berthels@fagg-afmps.be
Name of the EMA contact:	<b>Name : Leonor Enes</b> Email: Leonor.Enes@ema.europa.eu

## **Table of contents**

<b>1. Introduction .....</b>	<b>5</b>
1.1. Steps taken for the assessment .....	5
<b>2. Assessment of the post-authorisation measure P46 009 .....</b>	<b>5</b>
<b>3. Rapporteur's overall conclusion .....</b>	<b>6</b>

## 1. Introduction

This report covers the following post-authorisation commitments undertaken by the MAH:

Study D2560C00007 – a Phase 3 Open-label Study to Evaluate the Safety of MEDI3250 in Healthy Japanese Children aged 2 years through 6 years.

The rapporteur is of the opinion that the data do not support the requirement for a variation.

### 1.1. Steps taken for the assessment

Submission date:	
Start of procedure:	24/08/15
CHMP Rapporteur's preliminary assessment report circulated on:	28/09/15
CHMP Rapporteur's updated assessment report circulated on:	n/a
CHMP opinion:	22/10/15

## 2. Assessment of the post-authorisation measure P46 009

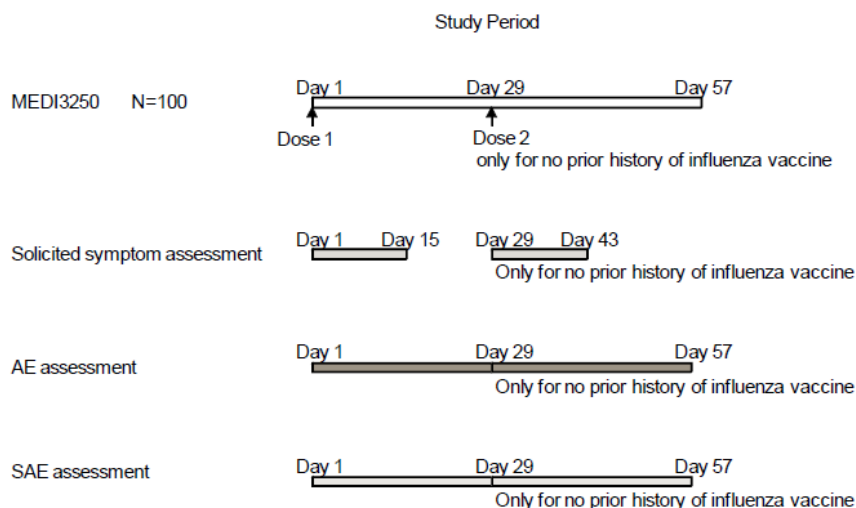
This open label, single arm, multicentre study enrolled 100 subjects. The study was designed to gather the safety and tolerability data in Japanese children 2 to 6 years of age that would support approval of MEDI3250 (Fluenz Tetra /FluMist Quadrivalent) in Japan.

For children age 2 years through 6 years, the recommended dosage schedule for intranasal administration was 0.2 mL (0.1 mL per nostril). For children not previously vaccinated against seasonal influenza, a second dose was recommended to be given after an interval of at least 4 weeks.

For the safety and tolerability endpoints, data were gathered on solicited symptoms, AEs and SAEs.

The study was conducted at 3 sites in Japan during the 2014/2015 influenza season. Study duration was 1 to 2 months for each participant. No subjects withdrew from the study or were excluded from the safety population.

Figure 1 Study flow chart



The median age of subjects was 4.5 years (mean  $\pm$  standard deviation [SD]: 4.2  $\pm$  1.4) and male subjects accounted for 45.0% (45 subjects). Ninety four subjects who had been previously vaccinated for seasonal influenza received one dose of the IP, and the remaining 6 subjects who had not been previously vaccinated for influenza received 2 doses of the IP with at least a 28 day- interval. A protocol deviation was reported in one subject with a GCP violation. No other protocol deviations or inappropriate treatment compliance including overdose were noted during the study.

The overall incidence of any solicited symptoms was 57.0% (57/100 subjects). The common solicited symptoms ( $\geq$  5%) were runny/stuffy nose (51.0%), cough (35.0%), fever  $\geq$  38.0°C (11.0%), sore throat (10.0%) and headache (5.0%).

42 out of 100 of subjects (42%) experienced at least one treatment-emergent adverse event (TEAEs) after the first dose, and 2 out of 6 subjects (33.3%) after the second dose.

The common TEAEs ( $\geq$  4%) reported during the study were nasopharyngitis (13.0%), gastroenteritis (4.0%), pharyngitis (4.0%), and dry skin (4.0%). No new TEAEs, by preferred term, were observed after the second dose. All TEAEs were graded as mild in severity. No deaths, SAEs or TEAEs leading to IP discontinuation were reported.

#### MAH's Conclusion

No novel safety signals were detected in this small study conducted in 100 Japanese children 2 through 6 years of age and the vaccine was safe and well tolerated. These data support the continued positive benefit/risk assessment for Fluenz Tetra.

### 3. Rapporteur's overall conclusion

Regarding the study, the Rapporteur notes that:

- The size of the sample permits to identify AEs with an incidence  $>$  2.5% with a probability of  $\geq$  90%;
- AEs solicited in the study are already rated in the SmPC to be common or very common. However, the frequency of AEs was not compared to the same frequency measured in similar studies. It is thus not possible to determine whether the reactogenicity during 2014/2015 season in the Japanese population was higher than the reactogenicity in other seasons or in

other populations. It is also not possible to confirm that other events, such as asthma or wheezing, are not more frequent than expected in the study population.

In consequence, although results are reassuring, no significant information is gained from this study.

The Rapporteur has no additional question to the MAH. No additional action is required.

PAM fulfilled (all commitments fulfilled) - No further action required

PAM not fulfilled (not all commitments fulfilled) and further action required: