EMA/85734/2020

European Medicines Agency decision

P/0065/2020

of 21 February 2020

on the acceptance of a modification of an agreed paediatric investigation plan for live, attenuated, chimeric dengue virus, serotype 1 / live, attenuated, chimeric dengue virus, serotype 2 / live, attenuated, chimeric dengue virus, serotype 3 / live, attenuated, chimeric dengue virus, serotype 4 (Dengvaxia), (EMEA-001545-PIP01-13-M02) in accordance with Regulation (EC) No 1901/2006 of the European Parliament and of the Council

Disclaimer

This decision does not constitute entitlement to the rewards and incentives referred to in Title V of Regulation (EC) No 1901/2006.

Only the English text is authentic.

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The European Medicines Agency,

Having regard to the Treaty on the Functioning of the European Union,

Having regard to Regulation (EC) No 1901/2006 of the European Parliament and of the Council of 12 December 2006 on medicinal products for paediatric use and amending Regulation (EEC) No. 1768/92, Directive 2001/20/EC, Directive 2001/83/EC and Regulation (EC) No 726/2004[1],

Having regard to Regulation (EC) No 726/2004 of the European Parliament and of the Council of 31 March 2004 laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency[2],

Having regard to the European Medicines Agency's decision P/0113/2014 issued on 5 May 2014 and the decision P/0174/2015 issued on 7 August 2015,

Having regard to the application submitted by Sanofi Pasteur SA on 25 October 2019 under Article 22 of Regulation (EC) No 1901/2006 proposing changes to the agreed paediatric investigation plan with a deferral and proposing a waiver,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 31 January 2020, in accordance with Article 22 of Regulation (EC) No 1901/2006 and Article 13 of said Regulation,

Having regard to Article 25 of Regulation (EC) No 1901/2006,

Whereas:

(1) The Paediatric Committee of the European Medicines Agency has given an opinion on the acceptance of changes to the agreed paediatric investigation plan and to the deferral and on the granting of a waiver.

(2) It is therefore appropriate to adopt a decision on the acceptance of changes to the agreed paediatric investigation plan, including changes to the deferral.

(3) It is therefore appropriate to adopt a decision granting a waiver.

[1] OJ L 378, 27.12.2006, p.1.
[2] OJ L 136, 30.4.2004, p. 1.

Has adopted this decision:

Article 1

Changes to the agreed paediatric investigation plan for live, attenuated, chimeric dengue virus, serotype 1 / Live, attenuated, chimeric dengue virus, serotype 2 / Live, attenuated, chimeric dengue virus, serotype 3 / Live, attenuated, chimeric dengue virus, serotype 4 (Dengvaxia), powder and solvent for suspension for injection, subcutaneous use, including changes to the deferral, are hereby accepted in the scope set out in the opinion of the Paediatric Committee of the European Medicines Agency annexed hereto, together with its appendices.

Article 2

A waiver for live, attenuated, chimeric dengue virus, serotype 1 / live, attenuated, chimeric dengue virus, serotype 2 / live, attenuated, chimeric dengue virus, serotype 3 / live, attenuated, chimeric dengue virus, serotype 4 (Dengvaxia), powder and solvent for suspension for injection, subcutaneous use, the details of which are set out in the opinion of the Paediatric Committee the European Medicines Agency annexed hereto, together with its appendices, is hereby granted.

Article 3

This decision is addressed to Sanofi Pasteur, 14 Espace Henry Vallee, 69007 - LYON, France.

EMA/PDCO/601099/2019
Amsterdam, 31 January 2020

Opinion of the Paediatric Committee on the acceptance of a modification of an agreed Paediatric Investigation Plan

EMEA-001545-PIP01-13-M02

Scope of the application

Active substance(s):

Live, attenuated, chimeric dengue virus, serotype 1 / Live, attenuated, chimeric dengue virus, serotype 2 / Live, attenuated, chimeric dengue virus, serotype 3 / Live, attenuated, chimeric dengue virus, serotype 4

Invented name:

Dengvaxia

Condition(s):

Prevention of dengue

Authorised indication(s):

See Annex II

Pharmaceutical form(s):

Powder and solvent for suspension for injection

Route(s) of administration:

Subcutaneous use

Name/corporate name of the PIP applicant:

Sanofi Pasteur SA

Information about the authorised medicinal product:

See Annex II

Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, Sanofi Pasteur SA submitted to the European Medicines Agency on 25 October 2019 an application for modification of the agreed paediatric investigation plan with a deferral as set out in the European Medicines Agency's decision P/0113/2014 issued on 5 May 2014 and the decision P/0174/2015 issued on 7 August 2015.

The application for modification proposed changes to the agreed paediatric investigation plan and to the deferral and proposed a waiver

The procedure started on 3 December 2019.

Scope of the modification

Some measures and timelines of the Paediatric Investigation Plan have been modified. A waiver for a new paediatric subset has been added.

Opinion

1. The Paediatric Committee, having assessed the application in accordance with Article 22 of Regulation (EC) No 1901/2006 as amended, recommends as set out in the appended summary report:

   - to agree to changes to the paediatric investigation plan and to the deferral in the scope set out in the Annex I of this opinion;
   - to grant a waiver for one or more subsets of the paediatric population concluded in accordance with Article 11(1)(a) of said Regulation, on the grounds that the specific medicinal product is likely to be ineffective or unsafe in part or all of the paediatric population.

   The Norwegian Paediatric Committee member agrees with the above-mentioned recommendation of the Paediatric Committee.

2. The measures and timelines of the paediatric investigation plan and the subset(s) of the paediatric population and condition(s) covered by the waiver are set out in the Annex I.

This opinion is forwarded to the applicant and the Executive Director of the European Medicines Agency, together with its annexes and appendix.

Annex I

The subset(s) of the paediatric population and condition(s) covered by the waiver and the measures and timelines of the agreed paediatric investigation plan (PIP)

1. Waiver

1.1. Condition:

Prevention of dengue

The waiver applies to:

- the paediatric population from birth to less than 9 months of age;
- powder and solvent for suspension for injection, subcutaneous use;
- on the grounds that the specific medicinal product is likely to be unsafe.

2. Paediatric Investigation Plan

2.1. Condition:

Prevention of dengue

2.1.1. Indication(s) targeted by the PIP

Active immunisation against dengue caused by dengue virus serotypes 1, 2, 3 and 4.

2.1.2. Subset(s) of the paediatric population concerned by the paediatric development

From 9 months to less than 18 years of age.

2.1.3. Pharmaceutical form(s)

Powder and solvent for suspension for injection.

2.1.4. Measures

Area	**Number of studies**	**Description**
Quality-related studies	0	Not applicable
Non-clinical studies	0	Not applicable
Clinical studies	15	**Study 1:** Randomised, observer-blind (first injection), open-label (second and third injections), controlled trial to evaluate safety, viraemia, humoral immune response, and persistence of antibodies to CYD dengue vaccine in healthy children from 2 to less than 18 years of age (CYD05)

		Study 2: Randomised, observer-blind (first injection), open-label (second and third injections), controlled trial to evaluate safety, viraemia, and humoral immune response to CYD dengue vaccine in healthy children from 2 to less than 18 years of age (CYD06) **Study 3:** Randomised, observer-blind (first and second injections), single-blind (third injection), controlled trial to evaluate humoral immune response to and safety of CYD dengue vaccine in healthy children from 9 to less than 17 years of age (CYD13) **Study 4:** Randomised, observer-blind, controlled trial to evaluate humoral immune response, safety, and viraemia following vaccination with CYD dengue vaccine in healthy children from 2 to less than 12 years of age previously vaccinated with yellow fever vaccine (CYD24) **Study 5:** Randomised, observer-blind, controlled trial to evaluate humoral immune response and safety of CYD dengue vaccine in healthy children from 9 to less than 17 years of age (CYD30) **Study 6:** Randomised, observer-blind (first injection), open-label (second and third injections), controlled trial to evaluate safety and viraemia following vaccination with CYD dengue vaccine, first dose co-administered or not with Measles, mumps, rubella (MMR) vaccine, in healthy children from 12 to less than 16 months of age (CYD08) **Study 7:** Randomised, observer-blind, placebo-controlled trial to evaluate safety and immunogenicity of CYD dengue vaccine in healthy children from 2 to less than 12 years of age (CYD32) **Study 8:** Randomised, observer-blind, controlled trial to evaluate efficacy of CYD dengue vaccine in healthy children from 4 to less than 12 years of age (CYD23) **Study 9:** 4-year follow-up to evaluate safety and the long-term follow-up of hospitalised dengue in children previously included in study CYD23 (CYD57) **Study 10:** Randomised, observer-blind, controlled trial to evaluate humoral immune response, safety, and persistence of antibodies to CYD dengue vaccine in healthy children from 2 to less than 18 years of age (CYD22)

		Study 11: Randomised, observer-blind (first injection), single-blind (second and third injection), controlled trial to evaluate safety and immunogenicity of CYD dengue vaccine in healthy children from 2 to less than 18 years of age (CYD28) **Study 12:** Randomised, observer-blind, placebo-controlled trial to evaluate efficacy of CYD dengue vaccine in healthy children from 2 to less than 15 years of age (CYD14) **Study 13:** Randomised, observer-blind, placebo-controlled trial to evaluate efficacy of CYD dengue vaccine in healthy children from 9 to less than 17 years of age (CYD15) **Study 14:** Randomised, observer-blind, placebo-controlled trial to evaluate the effect of co-administration of CYD dengue vaccine (first dose) on the immune response against yellow fever vaccine (YF) in flavivirus-naïve (at baseline) healthy children from 12 to 13 months of age (CYD29) **Study 15:** Randomised, observer-blind (second injection of CYD dengue vaccine), open-label (first and third injections of CYD dengue vaccine), placebo-controlled trial to evaluate the effect of co-administration of CYD dengue vaccine (second dose) on the immune response against a booster dose of DTaP-IPV//Hib vaccine in healthy children from 9 to less than 13 months of age (CYD33) **Study 16** This study was removed from the PIP during procedure EMEA-001545-PIP01-13-M02 **Study 17** This study was removed from the PIP during procedure EMEA-001545-PIP01-13-M02
Extrapolation, modelling & simulation studies	0	Not applicable
Other studies	0	Not applicable
Other measures	0	Not applicable

3. Follow-up, completion and deferral of PIP

Concerns on potential long term safety and efficacy issues in relation to paediatric use:	Yes
Date of completion of the paediatric investigation plan:	By June 2019
Deferral for one or more measures contained in the paediatric investigation plan:	Yes

Annex II

Information about the authorised medicinal product

Condition(s) and authorised indication(s):

1. Prevention of dengue disease

Authorised indication:

- Dengvaxia is indicated for the prevention of dengue disease caused by dengue virus serotypes 1, 2, 3 and 4 in individuals 9 to 45 years of age with prior dengue virus infection and living in endemic areas

Authorised pharmaceutical form(s):

Powder and solvent for suspension for injection

Authorised route(s) of administration:

Subcutaneous use