EMA/434507/2015

European Medicines Agency decision

P/0174/2015

of 7 August 2015

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 (EMEA-001545-PIP01-13-M01) 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,

Having regard to the application submitted by Sanofi Pasteur SA on 27 March 2015 under Article 22 of Regulation (EC) No 1901/2006 proposing changes to the agreed paediatric investigation plan with a deferral,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 19 June 2015, in accordance with Article 22 of Regulation (EC) No 1901/2006,

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.

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

[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, powder and solvent for suspension for injection, subcutaneous use, 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

This decision is addressed to Sanofi Pasteur SA, 2 avenue Pont Pasteur, 69007 – Lyon, France.

Done at London, 7 August 2015

For the European Medicines Agency
Jordi Llinares Garcia
Head of Division (ad interim)
Human Medicines Research and Development Support
(Signature on file)

EMA/PDCO/244051/2015
London, 19 June 2015

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

EMEA-001545-PIP01-13-M01

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

Condition(s):

Prevention of dengue

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

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 27 March 2015 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.

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

The procedure started on 21 April 2015.

Scope of the modification

Some measures of the Paediatric Investigation Plan have been modified.

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 in the scope set out in the Annex I of this opinion.

   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 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 annex 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

Not applicable.

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 birth 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	17	**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

Area	Number of studies	Description
		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)

Area	Number of studies	Description
		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:** Randomised, observer-blind, controlled trial to evaluate safety and humoral immune response to CYD dengue vaccine in healthy children from 6 to less than 16 months of age (CYD58). **Study 17:** Randomised, observer-blind, controlled trial to evaluate safety and humoral immune response of CYD dengue vaccine and the impact of presence of maternal antibodies on the vaccine response in healthy children from 0 (at enrolment) to less than 6 months of age (CYD61)
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:	No
Date of completion of the paediatric investigation plan:	By December 2024
Deferral for one or more measures contained in the paediatric investigation plan:	Yes