EMA/169096/2014

European Medicines Agency decision

P/0113/2014

of 5 May 2014

on the agreement of a paediatric investigation plan and on the granting of a deferral and on the refusal of 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 (EMEA-001545-PIP01-13) 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.

7 Westferry Circus ● Canary Wharf ● London E14 4HB ● United Kingdom
Telephone +44 (0)20 7418 8400 **Facsimile** +44 (0)20 7523 7040
E-mail info@ema.europa.eu **Website** www.ema.europa.eu

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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 application submitted by Sanofi Pasteur SA on 13 December 2013 under Article 16(1) of Regulation (EC) No 1901/2006 also requesting a deferral under Article 20 of said Regulation and a waiver under Article 13 of said Regulation,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 21 March 2014, in accordance with Article 18 of Regulation (EC) No 1901/2006, and Article 21 of said Regulation 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 agreement of a paediatric investigation plan and on the granting of a deferral and on the refusal of a waiver.

(2) It is therefore appropriate to adopt a decision agreeing a paediatric investigation plan.

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

(4) It is therefore appropriate to adopt a decision refusing 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

A 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, the details of which are set out in the opinion of the Paediatric Committee of the European Medicines Agency annexed hereto, together with its appendices, is hereby agreed.

Article 2

A deferral 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, the details of which are set out in the opinion of the Paediatric Committee of the European Medicines Agency annexed hereto, together with its appendices, is hereby granted.

Article 3

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, powder and solvent for suspension for injection, subcutaneous use, the details of which are set out in the opinion of the Paediatric Committee of the European Medicines Agency annexed hereto, together with its appendices, is hereby refused.

Article 4

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

Done at London, 5 May 2014

For the European Medicines Agency
Guido Rasi
Executive Director
(Signature on file)

EMA/PDCO/95820/2014 Corr

Opinion of the Paediatric Committee on the agreement of a Paediatric Investigation Plan and a deferral and on the refusal of a waiver

EMEA-001545-PIP01-13

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 16(1) of Regulation (EC) No 1901/2006 as amended, Sanofi Pasteur SA submitted for agreement to the European Medicines Agency on 13 December 2013 an application for a paediatric investigation plan for the above mentioned medicinal product and a deferral under Article 20 of said Regulation and a waiver under Article 13 of said Regulation.

The procedure started on 21 January 2014.

7 Westferry Circus ● Canary Wharf ● London E14 4HB ● United Kingdom
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E-mail info@ema.europa.eu **Website** www.ema.europa.eu

Opinion

1. The Paediatric Committee, having assessed the proposed paediatric investigation plan in accordance with Article 17 of Regulation (EC) No 1901/2006 as amended, recommends as set out in the appended summary report:

   - to agree the paediatric investigation plan in accordance with Article 18 of said Regulation;
   - to grant a deferral in accordance with Article 21 of said Regulation;
   - to refuse the granting of a waiver in accordance with Article 13 of said Regulation, for some of the subsets of the paediatric population and the above mentioned condition as it does not meet the grounds detailed in Article 11(1) of said Regulation.

   The Icelandic and the Norwegian Paediatric Committee members agree with the above-mentioned recommendation of the Paediatric Committee.

2. The measures and timelines of the agreed 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.

London, 21 March 2014

On behalf of the Paediatric Committee
Dr Dirk Mentzer, Chairman
(Signature on file)

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

1. Waiver

– ***Condition: prevention of dengue***

The request for the waiver applied to:

- the paediatric population from birth to less than 2 months of age;
- powder and solvent for suspension for injection, subcutaneous use;

The waiver request does not provide evidence to support the following grounds set out in Article 11(1) of Regulation (EC) No 1901/2006 that:

- (c) the specific medicinal product does not represent a significant therapeutic benefit over existing treatments for paediatric patients.

Because:

- the specific medicinal product may represent a significant therapeutic benefit as the needs are not met.

The waiver request is therefore refused by the PDCO.

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

Area	Number of studies	Description
		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

Area	Number of studies	Description
		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 (first and second injections of CYD dengue vaccine), open-label (third injection 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

Area	Number of studies	Description
		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