European Medicines Agency

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EUROPEAN MEDICINES AGENCY DECISION

of 16 June 2009

on the agreement of a Paediatric Investigation Plan and on the granting of a waiver for Human Papillomavirus1 Type 6 L1 protein / Human Papillomavirus1 Type 11 L1 protein / Human Papillomavirus1 Type 16 L1 protein / Human Papillomavirus1 Type 18 L1 protein (Silgard) (EMEA-000385-PIP01-08) in accordance with Regulation (EC) No 1901/2006 of the European Parliament and of the Council as amended

(ONLY THE ENGLISH TEXT IS AUTHENTIC)

DISCLAIMER: This Decision does not entitle to the rewards and incentives referred to in Title V of Regulation (EC) No 1901/2006, as amended.

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THE EUROPEAN MEDICINES AGENCY,

Having regard to the Treaty establishing the European Community,

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 as amended 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 Merck Sharp & Dohme (Europe) Inc on 9 September 2008 under Article 16(1) also requesting a waiver under Article 13 of said Regulation,

Having regard to the Opinion of the Paediatric Committee of the European Medicines Agency, issued on 30 April 2009, in accordance with Article 18 of Regulation (EC) No 1901/2006 as amended, and Article 13 of said Regulation**,**

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

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 waiver,

(2) It is therefore appropriate to adopt a Decision granting a Paediatric Investigation Plan.

(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

A Paediatric Investigation Plan for Human Papillomavirus1 Type 6 L1 protein / Human Papillomavirus1 Type 11 L1 protein / Human Papillomavirus1 Type 16 L1 protein / Human Papillomavirus1 Type 18 L1 protein (Silgard), suspension for injection, suspension for injection in pre-filled syringe, intramuscular 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 waiver for Human Papillomavirus1 Type 6 L1 protein / Human Papillomavirus1 Type 11 L1 protein / Human Papillomavirus1 Type 16 L1 protein / Human Papillomavirus1 Type 18 L1 protein (Silgard), suspension for injection, suspension for injection in pre-filled syringe, intramuscular 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

This decision is addressed to Merck Sharp & Dohme (Europe) Inc., Clos du Lynx 5, 1200 Brussels, Belgium

Done at London, 16 June 2009

For the European Medicines Agency
Thomas Lönngren
Executive Director

(Signature on file)

European Medicines Agency
Pre-authorisation Evaluation of Medicines for Human Use

Doc. Ref. EMEA/PDCO/228030/2009
EMEA-000385-PIP01-08

OPINION OF THE PAEDIATRIC COMMITTEE ON THE AGREEMENT OF A PAEDIATRIC INVESTIGATION PLAN AND A WAIVER

Scope of the application

Active substance(s):
Human Papillomavirus1 Type 6 L1 protein / Human Papillomavirus1 Type 11 L1 protein / Human Papillomavirus1 Type 16 L1 protein / Human Papillomavirus1 Type 18 L1 protein

(Invented) name:
Silgard

Condition(s):
Infection by Human Papillomavirus

Pharmaceutical form(s):
Suspension for injection
Suspension for injection in pre-filled syringe

Route(s) of administration:
Intramuscular use

Name/corporate name of the PIP applicant:
Merck Sharp & Dohme (Europe) Inc.

Information about the authorised medicinal product: see Annex II

Basis for opinion

Pursuant to Article 16(1) of Regulation (EC) No 1901/2006 as amended, Merck Sharp & Dohme (Europe) Inc. submitted for agreement to the EMEA on 9 September 2008 an application for a paediatric investigation plan for the above mentioned medicinal product and a waiver under Article 13 of said Regulation.

The procedure started on 16 October 2008.

Supplementary information was provided by the applicant on 20 February 2009.

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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 waiver for one or more subsets of the paediatric population in accordance with Article 13 of said Regulation and concluded in accordance with Article 11(1)(c) of said Regulation, on the grounds that the specific medicinal product does not represent a significant therapeutic benefit over existing treatments for paediatric patients.

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 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 Agency, together with its annex(es) and appendix.

London, 30 April 2009

On behalf of the Paediatric Committee
Dr Daniel Brasseur, Chairman

ANNEX I

THE MEASURES AND TIMELINES OF THE AGREED PAEDIATRIC INVESTIGATION PLAN AND THE SUBSET(S) OF THE PAEDIATRIC POPULATION AND CONDITION(S) COVERED BY THE WAIVER

A. CONDITION(S)

Infection by Human Papillomavirus

B. WAIVER

Infection by Human Papillomavirus

- **Condition**

The waiver applies to:

- the paediatric population from birth to less than 9 years of age for the suspension for injection and the suspension for injection in pre-filled syringe for intramuscular use

on the grounds that the specific medicinal product does not represent a significant therapeutic benefit over existing treatments.

C. PAEDIATRIC INVESTIGATION PLAN

- **Condition to be investigated**

Infection by Human Papillomavirus in males

- **Proposed PIP indication**

Prevention of premalignant genital lesions (cervical, vulvar, vaginal, anal, perineal, perianal, penile), cervical, anal, perineal, and perianal cancer, and external genital warts (condyloma acuminata) causally related to Human Papillomavirus (HPV) types 6, 11, 16 and 18 in males.

- **Subset(s) of the paediatric population concerned by the paediatric development**

From 9 to less than 18 years.

- **Formulation(s)**

Suspension for injection
Suspension for injection in pre-filled syringe

- **Studies**

Area	Number of studies	Description
Quality	0	Not applicable.
Non-clinical	0	Not applicable.
Clinical	1	Randomised, double-blind, placebo-controlled, multicentre trial to evaluate safety, immunogenicity and efficacy of Gardasil in male children from 16 to less than 18 years (and in adult subjects).

Measures to address long term follow-up of potential safety issues in relation to paediatric use:	No
Date of completion of the paediatric investigation plan:	By May 2010
Deferral for some or all studies contained in the paediatric investigation plan:	No

ANNEX II

INFORMATION ABOUT THE AUTHORISED MEDICINAL PRODUCT

EU Number	Invented name	Strength	Pharmaceutical Form	Route of Administration	Packaging	Content	Package size
EU/1/06/358/001	Silgard	--[1]	Suspension for injection	Intramuscular use	vial (glass)	0.5 ml	1 vial
EU/1/06/358/002	Silgard	--[1]	Suspension for injection	Intramuscular use	vial (glass)	0.5 ml	10 vials
EU/1/06/358/003	Silgard	--[1]	Suspension for injection	Intramuscular use	pre-filled syringe (glass)	0.5 ml	1 pre-filled syringe
EU/1/06/358/004	Silgard	--[1]	Suspension for injection	Intramuscular use	pre-filled syringe (glass)	0.5 ml	10 pre-filled syringes
EU/1/06/358/005	Silgard	--[1]	Suspension for injection	Intramuscular use	pre-filled syringe (glass)	0.5 ml	1 pre-filled syringe + 1 needle
EU/1/06/358/006	Silgard	--[1]	Suspension for injection	Intramuscular use	pre-filled syringe (glass)	0.5 ml	10 pre-filled syringes + 10 needles
EU/1/06/358/007	Silgard	--[1]	Suspension for injection	Intramuscular use	pre-filled syringe (glass)	0.5 ml	1 pre-filled syringe + 2 needles
EU/1/06/358/008	Silgard	--[1]	Suspension for injection	Intramuscular use	pre-filled syringe (glass)	0.5 ml	10 pre-filled syringes + 20 needles
EU/1/06/358/009	Silgard	--[1]	Suspension for injection	Intramuscular use	pre-filled syringe (glass)	0.5 ml	1 pre-filled syringe with needle guard
EU/1/06/358/010	Silgard	--[1]	Suspension for injection	Intramuscular use	pre-filled syringe (glass)	0.5 ml	10 pre-filled syringes with needle guard
EU/1/06/358/011	Silgard	--[1]	Suspension for injection	Intramuscular use	pre-filled syringe (glass)	0.5 ml	20 pre-filled syringes with needle guard
EU/1/06/358/012	Silgard	--[1]	Suspension for injection	Intramuscular use	pre-filled syringe (glass)	0.5 ml	1 pre-filled syringe with needle guard + 1 needle
EU/1/06/358/013	Silgard	--[1]	Suspension for injection	Intramuscular use	pre-filled syringe (glass)	0.5 ml	10 pre-filled syringes with needle guard + 10 needles
EU/1/06/358/014	Silgard	--[1]	Suspension for injection	Intramuscular use	pre-filled syringe (glass)	0.5 ml	20 pre-filled syringes with needle guard + 20 needles
EU/1/06/358/015	Silgard	--[1]	Suspension for injection	Intramuscular use	pre-filled syringe (glass)	0.5 ml	1 pre-filled syringe with needle guard + 2 needles
EU/1/06/358/016	Silgard	--[1]	Suspension for injection	Intramuscular use	pre-filled syringe (glass)	0.5 ml	10 pre-filled syringes with needle guard + 20 needles
EU/1/06/358/017	Silgard	--[1]	Suspension for injection	Intramuscular use	pre-filled syringe (glass)	0.5 ml	20 pre-filled syringes with needle guard + 40 needles
EU/1/06/358/018	Silgard	--[1]	Suspension for injection	Intramuscular use	vial (glass)	0.5 ml	20 vials

EU/1/06/358/019	Silgard	--[1]	Suspension for injection	Intramuscular use	pre-filled syringe (glass)	0.5 ml	20 pre-filled syringes
EU/1/06/358/020	Silgard	--[1]	Suspension for injection	Intramuscular use	pre-filled syringe (glass)	0.5 ml	20 pre-filled syringes + 20 needles
EU/1/06/358/021	Silgard	--[1]	Suspension for injection	Intramuscular use	pre-filled syringe (glass)	0.5 ml	20 pre-filled syringe + 40 needles

[1] 1 dose (0.5 ml) contains approximately:

Human Papillomavirus[1] Type 6 L1 protein[2], [3]	20 micrograms
Human Papillomavirus[1] Type 11 L1 protein[2], [3]	40 micrograms
Human Papillomavirus[1] Type 16 L1 protein[2], [3]	40 micrograms
Human Papillomavirus[1] Type 18 L1 protein[2], [3]	20 micrograms

[1] Human Papillomavirus = HPV
[2] L1 protein in the form of virus-like particles produced in yeast cells (Saccharomyces cerevisiae CANADE 3C-5 (Strain 1895)) by recombinant DNA technology
[3] adsorbed on amorphous aluminium hydroxyphosphate sulphate adjuvant (225 micrograms Al)