Fendrix

Procedural steps taken and scientific information after the authorisation

Application number	Scope	Opinion / Notification [1] issued on	Commission Decision Issued [2] / amended on	Product Information affected [3]	Summary
WS/1223	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS	09/11/2017	n/a		

[1] Notifications are issued for type I variations and Article 61(3) notifications (unless part of a group including a type II variation or extension application or a worksharing application). Opinions are issued for all other procedures.
[2] A Commission decision (CD) is issued for procedures that affect the terms of the marketing authorisation (e.g. summary of product characteristics, annex II, labelling, package leaflet). The CD is issued within two months of the opinion for variations falling under the scope of Article 23.1a(a) of Regulation (EU) No. 712/2012, or within one year for other procedures.
[3] SmPC (Summary of Product Characteristics), Annex II, Labelling, PL (Package Leaflet).

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N/0060	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	27/10/2017		Labelling	
IG/0811	B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure	19/06/2017	n/a		
IG/0738	B.I.b.1.d - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Deletion of a non-significant specification parameter (e.g. deletion of an obsolete parameter)	16/12/2016	n/a		
WS/1007	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. B.I.b.2.e - Change in test procedure for AS or starting material/reagent/intermediate - Other changes to a test procedure (including replacement or addition) for the AS or a starting material/intermediate	15/12/2016	n/a		
WS/1009	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. B.II.d.2.z - Change in test procedure for the finished product - Other variation	10/11/2016	n/a		
IA/0055	B.II.b.5.b - Change to in-process tests or limits applied during the manufacture of the finished	29/09/2016	n/a		

	product - Addition of a new test(s) and limits				
IG/0719/G	This was an application for a group of variations. B.II.e.2.b - Change in the specification parameters and/or limits of the immediate packaging of the finished product - Addition of a new specification parameter to the specification with its corresponding test method B.II.e.2.b - Change in the specification parameters and/or limits of the immediate packaging of the finished product - Addition of a new specification parameter to the specification with its corresponding test method B.II.e.2.b - Change in the specification parameters and/or limits of the immediate packaging of the finished product - Addition of a new specification parameter to the specification with its corresponding test method B.II.e.6.b - Change in any part of the (primary) packaging material not in contact with the finished product formulation - Change that does not affect the product information	21/09/2016	n/a		
PSUSA/1598/201602	Periodic Safety Update EU Single assessment - hepatitis B (rDNA) vaccine (adjuvanted, adsorbed)	02/09/2016	n/a		PRAC Recommendation - maintenance
WS/0843	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. B.II.c.2.z - Change in test procedure for an excipient	21/04/2016	n/a		

	- Other variation				
WS/0864	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. B.I.b.2.e - Change in test procedure for AS or starting material/reagent/intermediate - Other changes to a test procedure (including replacement or addition) for the AS or a starting material/intermediate	25/02/2016	n/a		
IA/0050	B.II.b.3.a - Change in the manufacturing process of the finished or intermediate product - Minor change in the manufacturing process	28/01/2016	n/a		
N/0048	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	12/11/2015		PL	
WS/0817/G	This was an application for a group of variations following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. A.4 - Administrative change - Change in the name and/or address of a manufacturer or an ASMF holder or supplier of the AS, starting material, reagent or intermediate used in the manufacture of the AS or manufacturer of a novel excipient A.7 - Administrative change - Deletion of manufacturing sites B.I.a.1.f - Change in the manufacturer of AS or of a	29/10/2015	n/a		

	starting material/reagent/intermediate for AS - Changes to quality control testing arrangements for the AS -replacement or addition of a site where batch control/testing takes place				
II/0046/G	This was an application for a group of variations. B.II.b.1.c - Replacement or addition of a manufacturing site for the FP - Site where any manufacturing operation(s) take place, except batch release/control, and secondary packaging, for biol/immunol medicinal products or pharmaceutical forms manufactured by complex manufacturing processes B.II.e.1.b.2 - Change in immediate packaging of the finished product - Change in type/addition of a new container - Sterile medicinal products and biological/immunological medicinal products	24/09/2015	n/a		
WS/0728	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. B.I.b.2.z - Change in test procedure for AS or starting material/reagent/intermediate - Other variation	25/06/2015	n/a		
WS/0734	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. B.II.c.z - Change in control of excipients in the	25/06/2015	n/a		

	Finished Product - Other variation				
WS/0610/G	This was an application for a group of variations following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. B.I.b.2.d - Change in test procedure for AS or starting material/reagent/intermediate - Substantial change to or replacement of a biological/immunological/immunochemical test method or a method using a biological reagent for a biological AS B.II.b.5.b - Change to in-process tests or limits applied during the manufacture of the finished product - Addition of a new test(s) and limits	22/01/2015	n/a		
WS/0603	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. B.II.c.1.z - Change in the specification parameters and/or limits of an excipient - Other variation	20/11/2014	n/a		
WS/0591	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. Submission of final study report of a post-approval clinical study to compare the current and the new plunger stoppers and tip caps in response to a CHMP recommendation.	20/11/2014	n/a		

	C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority				
R/0034	Renewal of the marketing authorisation.	25/09/2014	17/11/2014	SmPC and PL	The previously established favourable benefit-risk profile for Fendrix, indicated for active immunisation against hepatitis B infection, remains unchanged with reference to both the efficacy and safety data that have become available during the time period covered by this renewal application. The CHMP therefore recommended that the renewal be granted with unlimited validity.
WS/0593	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. B.II.d.1.c - Change in the specification parameters and/or limits of the finished product - Addition of a new specification parameter to the specification with its corresponding test method	23/10/2014	n/a		
PSUV/0037	Periodic Safety Update	11/09/2014	n/a		PRAC Recommendation - maintenance
WS/0515	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure	26/06/2014	n/a		

WS/0553	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. B.II.d.2.d - Change in test procedure for the finished product - Other changes to a test procedure (including replacement or addition)	26/06/2014	n/a		
WS/0426/G	This was an application for a group of variations following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. B.I.a.2.c - Changes in the manufacturing process of the AS - The change refers to a [-] substance in the manufacture of a biological/immunological substance which may have a significant impact on the medicinal product and is not related to a protocol B.I.a.3.e - Change in batch size (including batch size ranges) of AS or intermediate - The scale for a biological/immunological AS is increased/decreased without process change (e.g. duplication of line)	26/06/2014	n/a		
IB/0039	B.II.d.2.d - Change in test procedure for the finished product - Other changes to a test procedure (including replacement or addition)	25/06/2014	n/a		
IG/0446	C.I.8.a - Introduction of or changes to a summary of Pharmacovigilance system - Changes in QPPV (including contact details) and/or changes in the PSMF location	24/06/2014	n/a		

II/0032	B.II.b.1.c - Replacement or addition of a manufacturing site for the FP - Site where any manufacturing operation(s) take place, except batch release/control, and secondary packaging, for biol/immunol medicinal products or pharmaceutical forms manufactured by complex manufacturing processes	22/05/2014	n/a		
WS/0415	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. Change in specifications of active substance. B.I.b.1.f - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Change outside the approved specifications limits range for the AS	23/01/2014	n/a		
IAIN/0031	C.I.10 - Change in the frequency and/or date of submission of PSURs for human medicinal products	19/12/2013	17/11/2014	Annex II	
IG/0306	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	12/06/2013	n/a		
IB/0027	B.II.b.1.f - Replacement or addition of a manufacturing site for part or all of the manufacturing process of the FP - Site where any manufacturing operation(s) take place, except batch release, batch control, and secondary packaging, for sterile medicinal products (including those that are aseptically manufactured) excluding biological/	31/05/2013	n/a		

	immunological medicinal products				
IB/0025	B.II.c.1.z - Change in the specification parameters and/or limits of an excipient - Other variation	30/04/2013	n/a		
IG/0297	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	19/04/2013	n/a		
II/0024	Replacement of the current screwcaps used for the purified bulk transfer and storage. B.I.c.1.b - Change in immediate packaging of the AS - Qualitative and/or quantitative composition for sterile and non-frozen biological/immunological ASs	21/02/2013	n/a		
WS/0336	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. To introduce a new method for monitoring homogeneity during filling. B.II.b.5.z - Change to in-process tests or limits applied during the manufacture of the finished product - Other variation	17/01/2013	n/a		
WS/0304	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. To introduce an additional method for identification of the Master and Working Seeds used for the	18/10/2012	18/10/2012		

	manufacture of MPL. B.I.b.2.d - Change in test procedure for AS or starting material/reagent/intermediate - Change (replacement) to a biological/immunological/ immunochemical test method or a method using a biological reagent for a biological AS				
IG/0170/G	This was an application for a group of variations. B.I.a.4.c - Change to in-process tests or limits applied during the manufacture of the AS - Deletion of a non-significant in-process test B.I.a.4.a - Change to in-process tests or limits applied during the manufacture of the AS - Tightening of in-process limits	25/04/2012	n/a		
WS/0201/G	This was an application for a group of variations following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. To propose new target fill volume controls. To align the volume specifications to be applied at release and during stability evaluation. To revise QC release procedures for final container volume determination. B.II.d.1.z - Change in the specification parameters and/or limits of the finished product - Other variation B.II.b.3.b - Change in the manufacturing process of the finished product - Substantial changes to a	19/01/2012	n/a		

	manufacturing process that may have a significant impact on the quality, safety and efficacy of the medicinal product B.II.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test procedure				
WS/0153	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. This was an application for a group of variations following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. Update of section 4.4 of the SmPC to include a warning on psychogenic syncope based on the available safety data. The PL was proposed to be updated in accordance. In addition, the company took the opportunity to update the list of local representatives in the PL of Pumarix, Ambirix, Pandemrix, Pandemic influenza vaccine (H5N1) (split virion, inactivated, adjuvanted) GlaxoSmithKline Biologicals, Prepandrix and Fendrix. C.I.4 - Variations related to significant modifications of the SPC due in particular to new quality, pre-clinical, clinical or pharmacovigilance data	17/11/2011	19/12/2011	SmPC and PL	Based on a review of literature and a search in the global safety database performed by the MAH, the CHMP recommended including a wording on psychogenic syncope to the product information of the MAH injectable vaccines. The literature review showed an incidence peak occurred around the age of 15 years, with females having more than twice the incidence of males. The syncope reports with secondary injuries were reported most frequently in children and adolescents. Given that psychogenic syncope is not a true side effect, it was not considered appropriate to include syncope as an undesirable effect in section 4.8 of the SmPC. However, as such events can result in injury, and may not have occurred in the absence of the vaccination, the CHMP recommended to add a reference to such events in section 4.4 'Warning and Precaution' of the SmPC and in the PL.
IG/0080	B.II.c.2.a - Change in test procedure for an excipient - Minor changes to an approved test procedure	01/07/2011	n/a		

IG/0064/G	This was an application for a group of variations. Update of section 4.8 of the SmPC to include immediate injection site pain, stinging and burning sensation. The PL is updated in accordance. The MAH has also taken the opportunity to align section 4.6 of the prefilled syringe presentation with the vial presentation. Furthermore, the Labelling is updated to specify the container 'prefilled syringe'. In addition, the MAH has taken the opportunity to update the list of local representatives in the PL. B.II.e.2.a - Change in the specification parameters and/or limits of the immediate packaging of the finished product - Tightening of specification limits B.II.e.2.b - Change in the specification parameters and/or limits of the immediate packaging of the finished product - Addition of a new specification parameter to the specification with its corresponding test method B.II.e.3.a - Change in test procedure for the immediate packaging of the finished product - Minor changes to an approved test procedure B.II.e.3.c - Change in test procedure for the immediate packaging of the finished product - Deletion of a test procedure if an alternative test procedure is already authorised B.II.e.6.b - Change in any part of the (primary) packaging material not in contact with the finished product formulation - Change that does not affect the product information B.II.e.7.a - Change in supplier of packaging	04/05/2011	n/a		Following clusters of spontaneous reports of immediate onset injection site pain reported in certain batches of the preservative-free formulation of Twinrix Adult, immediate pain, stinging and burning at the injection site has been reflected in section 4.8 of the SmPC and section 4 of the package leaflet. The MAH's investigation report revealed no specific root cause for the clusters of reports of immediate injection site pain. The injection site reactions were non-serious and self-limited in all cases. The benefit-risk of Twinrix Adult remains positive.

	components or devices (when mentioned in the dossier) - Deletion of a supplier				
II/0014	To update section 4.8 of the SmPC to modify the frequency classification of allergic reactions as per request of the CHMP. Section 4 of the PL is updated accordingly. The SmPC is also updated according to the SmPC guideline and QRD template. Furthermore, the MAH takes the opportunity to update the PL based on the readability testing results. C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	24/06/2010	28/07/2010	SmPC and PL	Taking into account the relatively low vaccine exposure reported with Fendrix and the fact that anaphylactoid reactions have occurred with other hepatitis B vaccines, the CHMP considered that "anaphylactoid reactions" should continue to be reflected in section 4.8 of the SmPC. In addition, changes to the PL of Fendrix according to the results of the readability testing have been introduced.
WS/0001	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. To register an additional building for formulation activities. B.II.b.1.c - Replacement or addition of a manufacturing site for the FP - Site where any manufacturing operation(s) take place, except batch release, batch control, and secondary packaging, for biological/immunological medicinal products.	22/04/2010	n/a		
R/0012	Renewal of the marketing authorisation.	24/09/2009	10/12/2009		
IB/0013	IB_12_a_Change in spec. of active subst./agent used in manuf. of active subst. - tightening	18/08/2009	n/a		

II/0010	Change to the primary pack stopper and tip cap for pre-filled syringes. Change(s) to the manufacturing process for the finished product	25/06/2009	30/06/2009		
II/0009	Change to the manufacturing process for the active substance . Change(s) to the manufacturing process for the active substance	29/05/2009	05/06/2009		
IA/0011	IA_09_Deletion of manufacturing site	07/05/2009	n/a		
II/0008	A scale up the manufacture of adjuvant MPL liquid bulk. Change(s) to the manufacturing process for the finished product	23/04/2009	27/04/2009		
II/0007	Registration of thiomersal free (TF) hepatitis B antigen. Change(s) to the manufacturing process for the active substance	22/01/2009	02/03/2009	SmPC, Annex II, Labelling and PL	
II/0006	Update of the quality information for the MPL (3-O-deacyl-4'-monophosphoryl lipid A) component of the adjuvant system used for Fendrix. Change(s) to the manufacturing process for the finished product	22/01/2009	27/01/2009		

II/0005	Change(s) to the test method(s) and/or specifications for the active substance	26/04/2007	03/05/2007		
II/0004	Change(s) to the manufacturing process for the finished product	16/11/2006	22/11/2006		
N/0003	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	07/02/2006	n/a	Labelling and PL	
II/0002	Change(s) to the test method(s) and/or specifications for the finished product	17/11/2005	22/11/2005		
II/0001	Change(s) to the test method(s) and/or specifications for the active substance Change(s) to the test method(s) and/or specifications for the finished product	15/09/2005	26/09/2005		