EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Tritanrix HepB

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/0401	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	25/07/2013	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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IG/0306	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	12/06/2013	n/a		
IG/0297	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	19/04/2013	n/a		
II/0063	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/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 manufacturing process that may have a significant	19/01/2012	n/a		

	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				
IG/0052/G	This was an application for a group of variations. 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.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.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.c - Change in the specification parameters and/or limits of the immediate packaging of the finished product - Deletion of a non-significant specification parameter (e.g. deletion of an obsolete parameter) 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	18/03/2011	n/a		

	finished product - Addition of a new specification parameter to the specification with its corresponding test method B.II.e.2.c - Change in the specification parameters and/or limits of the immediate packaging of the finished product - Deletion of a non-significant specification parameter (e.g. deletion of an obsolete parameter)				
II/0057	Changes to the manufacturing process of the diphteria drug substance. 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 medicinal product and is not related to a protocol	21/10/2010	27/10/2010		
IB/0058	Change in a test procedure for the master and working seeds of Clostridium tetani and Corynebacterium dipheriae. 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	11/08/2010	n/a		
IB/0059	Change in an in-process test for the active substance. B.I.a.4.z - Change to in-process tests or limits applied during the manufacture of the AS - Other variation	11/08/2010	n/a		
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.	22/04/2010	22/04/2010		

	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. 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.				
IB/0056	IB_12_a_Change in spec. of active subst./agent used in manuf. of active subst. - tightening	18/09/2009	n/a		
II/0055	Introduction of new filter equipment during the manufacturing process of tetanus toxoid. Change(s) to the manufacturing process for the active substance	25/06/2009	02/07/2009		
II/0053	Change to the purification process of diphteria (D) and tetanus (T) toxoid. Change(s) to the manufacturing process for the active substance	19/03/2009	25/03/2009		
II/0054	Modification of the purification process for tetanus toxoid. Change(s) to the manufacturing process for the active substance	19/03/2009	25/03/2009		
II/0052	Change in the production process for the whole cell pertussis concentrate produced by Novartis Vaccines & Diagnostics GmbH &Co. Change(s) to the manufacturing process for the active substance	22/01/2009	28/01/2009		

II/0049	Update of Summary of Product Characteristics and Package Leaflet	18/12/2008	27/01/2009	SmPC and PL	
II/0047	Change to the shelf-life specification of thiomersal for the two-dose and multi-dose presentations of Tritanrix HepB. Change(s) to the test method(s) and/or specifications for the finished product	20/11/2008	26/11/2008		
IA/0050	IA_04_Change in name and/or address of a manuf. of the active substance (no Ph. Eur. cert. avail.)	21/11/2008	n/a	Annex II	
IA/0051	IA_25_b_01_Change to comply with Ph. - compliance with EU Ph. update - active substance	18/11/2008	n/a		
II/0048	Extension of the shelf life for the DTPw bulk, used in the formulation of Tritanrix HepB. Change(s) to the manufacturing process for the active substance	25/09/2008	01/10/2008		
IA/0046	IA_05_Change in the name and/or address of a manufacturer of the finished product	18/07/2008	n/a		
IA/0045	IA_12_a_Change in spec. of active subst./agent used in manuf. of active subst. - tightening of spec.	07/07/2008	n/a		
II/0044	To update section 4.8 of the SPC to bring it in line with the current SPC guideline. Update of Summary of Product Characteristics	19/03/2008	22/04/2008	SmPC	The undesirable effects section was reviewed to bring it in line with the current SPC guideline. The section was restructured so that the adverse events were listed under the appropriate heading. The frequency of all events remained the same but these were aligned in order of decreasing seriousness.
II/0043	Update of Summary of Product Characteristics. Update of sections 4.4 and 4.8 of the SPC to implement the class labelling text on the risk of apnoea following vaccination of very prematurely born infants agreed by the CHMP in July 2007.	15/11/2007	06/12/2007	SmPC	Following a review on the risk of apnoea in very premature infants after immunisation the CHMP recommended a class labelling on apnoea for all vaccines in very premature infants. The SPC was updated to include information about the

	Update of Summary of Product Characteristics				potential risk of apnoea and the need for respiratory monitoring for 48-72h, when the primary immunisation series is administered to very premature infants (born ? 28 weeks of gestation) and particularly for those with a previous history of respiratory immaturity. Nonetheless, preterm infants should not be withdrawn from the immunisation scheme because the benefit of vaccination outweighs the risk of apnoea.
II/0041	Change(s) to the manufacturing process for the active substance	20/09/2007	24/10/2007	SmPC, Labelling and PL	
II/0042	To update section 5.1 of the SPC to include information about the immune response induced by the 6, 10, 14-week schedule further to the assessment of the renewal. Section 4.2 was consequently updated to include the administration of a dose of hepatitis B vaccine at birth when the vaccine is given according to this schedule. In addition the MAH completed the list of local representatives in the PL to include the two new EU Member States (Bulgaria and Romania) and updated the SPC, annex II and PL according to the latest EMEA/QRD template. Update of Summary of Product Characteristics and Package Leaflet	21/06/2007	10/08/2007	SmPC, Annex II and PL	The product information was updated to reflect information from clinical studies performed with the 6-10-14 weeks schedule for Tritanrix Hep B. The data showed that when this schedule is to be used, it is recommended to administer a dose of hepatitis B vaccine at birth to improve protection. Other changes were introduced to the product information to bring it in line with the current templates.
II/0040	Change(s) to the manufacturing process for the finished product	16/11/2006	27/11/2006		
R/0039	Renewal of the marketing authorisation.	01/06/2006	28/07/2006	SmPC, Annex II, Labelling and PL	

II/0033	Change(s) to the manufacturing process for the active substance	27/04/2006	03/05/2006		
N/0038	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	13/10/2005	n/a	Labelling and PL	
IB/0037	IB_37_b_Change in the specification of the finished product - add. of new test parameter	28/09/2005	n/a		
II/0036	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		
II/0034	Change(s) to the test method(s) and/or specifications for the finished product	16/03/2005	23/03/2005		
II/0035	Change(s) to the test method(s) and/or specifications for the finished product	16/03/2005	23/03/2005		
IB/0032	IB_38_b_Change in test procedure of finished product - minor change, biol. active subst./excipient	02/12/2004	n/a		
II/0031	Change(s) to the manufacturing process for the active substance	16/09/2004	21/09/2004		
II/0029	Update of section 4.8 following the assessment of PSUR 10, to include hypotonic-hyporesponsive episodes. The Package Leaflet (PL) was also updated to reflect the information on the SPC. Update of Summary of Product Characteristics and Package Leaflet	22/04/2004	17/06/2004	SmPC and PL	Based on the assessment of PSUR 10 covering the period from 20.07.02 to 19.07.03, the CHMP agreed that the MAH should update section 4.8 (Undesirable effects) to include very rare reports of hypotonic-hyporesponsive episodes. In addition, the CHMP agreed with the MAH proposal to complete the list of local representatives in the PL in order to include the 10 accession countries and amend the declarations of storage conditions in SPC section 6.4 (Special Precautions for storage), PL and labelling in accordance with EMEA/QRD templates.
IA/0030	IA_05_Change in the name and/or address of a manufacturer of the finished product	12/03/2004	n/a		
N/0028	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	06/08/2003	03/10/2003	Labelling and	

				PL	
I/0027	01_Change in or addition of manufacturing site(s) for part or all of the manufacturing process	22/07/2003	25/07/2003		
II/0021	Change(s) to the test method(s) and/or specifications for the active substance	20/02/2003	04/03/2003		
N/0025	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	19/09/2002	10/10/2002	PL	
II/0019	Quality: Change(s) to the manufacturing process for the active substance Quality: Change(s) to the manufacturing process for the finished product Change(s) to the test method(s) and/or specifications for the finished product	19/09/2002	25/09/2002		
I/0018	03_Change in the name and/or address of the marketing authorisation holder 01_Change following modification(s) of the manufacturing authorisation(s)	05/11/2001	29/01/2002	SmPC, Annex II, Labelling and PL	
I/0017	01_Change in the name of a manufacturer of the medicinal product	16/11/2001	06/12/2001		
R/0014	Renewal of the marketing authorisation.	26/07/2001	20/11/2001	SmPC, Annex II, Labelling and PL	
II/0015	Quality changes	20/09/2001	08/10/2001		
II/0013	Update of or change(s) to the pharmaceutical documentation	23/08/2001	07/09/2001		
I/0016	01_Change following modification(s) of the manufacturing authorisation(s)	22/08/2001	n/a		
N/0012	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	20/03/2001	17/05/2001	Labelling	
II/0010	New presentation(s)	25/01/2001	03/05/2001	SmPC,	

				Labelling and PL	
II/0009	Update of Summary of Product Characteristics and Package Leaflet	19/10/2000	13/03/2001	SmPC and PL	
II/0011	Change(s) to the test method(s) and/or specifications for the finished product	25/01/2001	01/02/2001		
I/0008	25_Change in test procedures of the medicinal product	16/03/2000	n/a		
I/0006	13_Batch size of active substance	29/07/1999	04/08/1999		
I/0007	12_Minor change of manufacturing process of the active substance	29/07/1999	04/08/1999		
II/0005	Change(s) to shelf-life or storage conditions	23/06/1999	23/06/1999		
N/0004	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	04/09/1998	n/a	PL	
I/0002	02_Change in the name of the medicinal product (either invented name of common name)	20/08/1997	12/12/1997	SmPC, Labelling and PL	
I/0003	01_Change in the name of a manufacturer of the medicinal product	31/10/1997	n/a		
I/0001	20_Extension of shelf-life as foreseen at time of authorisation	03/07/1997	25/09/1997	SmPC	