



## Hexyon

### Procedural steps taken and scientific information after the authorisation

Application number	Scope	Opinion/ Notification <sup>1</sup> issued on	Commission Decision Issued <sup>2</sup> / amended on	Product Information affected <sup>3</sup>	Summary
WS/2345	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.4.c - Change to in-process tests or limits applied during the manufacture of the AS - Deletion of a	08/12/2022	n/a		

<sup>1</sup> 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.

<sup>2</sup> 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.

<sup>3</sup> SmPC (Summary of Product Characteristics), Annex II, Labelling, PL (Package Leaflet).



	non-significant in-process test				
PSUSA/10091 /202204	Periodic Safety Update EU Single assessment - diphtheria / tetanus / pertussis antigens (pertussis toxoid, filamentous haemagglutinin) (acellular, component) / hepatitis b (rdna) / poliomyelitis (inactivated) / haemophilus type b conjugate vaccines (adsorbed)	01/12/2022	n/a		PRAC Recommendation - maintenance
WS/2239/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.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS	01/12/2022	n/a		
N/0143	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	08/11/2022		Labelling and PL	
IG/1559	B.IV.1.a.1 - Change of a measuring or administration device - Addition or replacement of a device which is not an integrated part of the primary packaging - Device with CE marking	24/10/2022	n/a		
WS/2309/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.	22/09/2022		SmPC and PL	

	<p>B.II.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test procedure</p> <p>B.II.d.1.e - Change in the specification parameters and/or limits of the finished product - Change outside the approved specifications limits range</p>				
WS/2313	<p>This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.</p> <p>B.II.d.2.c - Change in test procedure for the finished product - Substantial change to or replacement of a biol/immunol/immunochemical test method or a method using a biol. reagent or replacement of a biol. reference preparation not covered by an approved protocol</p>	15/09/2022	n/a		
WS/2138/G	<p>This was an application for a group of variations following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.</p> <p>B.II.d.1.z - Change in the specification parameters and/or limits of the finished product - Other variation</p> <p>B.II.d.2.c - Change in test procedure for the finished product - Substantial change to or replacement of a biol/immunol/immunochemical test method or a method using a biol. reagent or replacement of a biol. reference preparation not covered by an approved protocol</p>	01/09/2022	n/a		

WS/2282	<p>This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.</p> <p>B.I.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation</p>	21/07/2022	n/a		
WS/2272/G	<p>This was an application for a group of variations following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.</p> <p>B.I.b.2.z - Change in test procedure for AS or starting material/reagent/intermediate - Other variation  B.I.b.1.c - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Addition of a new specification parameter to the specification with its corresponding test method</p>	07/07/2022	n/a		
WS/2262	<p>This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.</p> <p>B.I.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation</p>	23/06/2022	n/a		
WS/2245	<p>This was an application for a variation following a worksharing procedure according to Article 20 of</p>	02/06/2022	n/a		

	<p>Commission Regulation (EC) No 1234/2008.</p> <p>B.II.b.3.b - Change in the manufacturing process of the finished or intermediate product - Substantial changes to a manufacturing process that may have a significant impact on the quality, safety and efficacy of the medicinal product</p>				
WS/2233	<p>This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.</p> <p>B.II.c.1.z - Change in the specification parameters and/or limits of an excipient - Other variation</p>	22/04/2022	n/a		
WS/2174	<p>This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.</p> <p>Update of section 4.5 of the SmPC in order to add drug-drug interaction information regarding the co-administration of Hexyon / Hexacima with varicella vaccines based on a re-analysis of the A3L15 clinical trial varicella serological data, submitted in the initial CTD dossier. The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to correct some typo errors in the SmPC and PL.</p> <p>C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data</p>	24/03/2022		SmPC and PL	<p>The MAH presented a new analysis of the serological data of clinical study A3L15(based on a different definition for seroresponse) on the co-administration of varicella vaccines with the hexavalent DTaP-IPVHB-PRP~Ta vaccines Hexacima and Hexyon. This analysis showed that these vaccines can be co-administered with varicella vaccines.</p> <p>The Product information for Hexacima and Hexyon has been updated to reflect the above findings.</p> <p>For more information, please refer to the Summary of Product Characteristics.</p>

WS/2148/G	<p>This was an application for a group of variations following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.</p> <p>B.III.1.b.3 - Submission of a new/updated or deletion of Ph. Eur. TSE Certificate of Suitability - Updated certificate from an already approved manufacturer</p> <p>B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure</p> <p>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</p>	10/02/2022	n/a		
WS/2188/G	<p>This was an application for a group of variations following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.</p> <p>B.I.b.1.g - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Widening of the approved specs for starting mat./intermediates, which may have a significant effect on the quality of the AS and/or the FP</p> <p>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</p>	13/01/2022	n/a		

	biological AS				
IG/1465	B.III.2.b - Change to comply with Ph. Eur. or with a national pharmacopoeia of a Member State - Change to comply with an update of the relevant monograph of the Ph. Eur. or national pharmacopoeia of a Member State	14/12/2021	n/a		
WS/2139	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	02/12/2021	n/a		
N/0129	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	15/11/2021		PL	
WS/2112	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	28/10/2021	n/a		
WS/2101	This was an application for a variation following a worksharing procedure according to Article 20 of	02/09/2021	n/a		

	<p>Commission Regulation (EC) No 1234/2008.</p> <p>B.I.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation</p>				
WS/2080/G	<p>This was an application for a group of variations following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.</p> <p>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</p> <p>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)</p> <p>B.I.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation</p> <p>B.I.b.1.b - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Tightening of specification limits</p> <p>B.I.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation</p>	22/07/2021	n/a		



WS/2033	<p>This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.</p> <p>B.I.a.4.z - Change to in-process tests or limits applied during the manufacture of the AS - Other variation</p>	24/06/2021	n/a		
WS/1930	<p>This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.</p> <p>B.I.a.1.z - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Other variation</p>	28/05/2021	n/a		
WS/2034	<p>This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.</p> <p>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</p>	15/04/2021	n/a		
WS/2005/G	<p>This was an application for a group of variations following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.</p> <p>B.I.b.1.b - Change in the specification parameters and/or limits of an AS, starting</p>	18/03/2021	n/a		

	<p>material/intermediate/reagent - Tightening of specification limits</p> <p>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</p>				
WS/2001	<p>This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.</p> <p>B.II.d.1.f - Change in the specification parameters and/or limits of the finished product - Deletion of a specification parameter which may have a significant effect on the overall quality of the finished product</p>	11/03/2021	n/a		
WS/1926/G	<p>This was an application for a group of variations following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.</p> <p>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</p> <p>B.I.b.1.b - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Tightening of specification limits</p> <p>B.I.b.1.z - Change in the specification parameters and/or limits of an AS, starting</p>	25/02/2021	n/a		

	<p>material/intermediate/reagent - Other variation</p> <p>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</p> <p>B.III.2.b - Change to comply with Ph. Eur. or with a national pharmacopoeia of a Member State - Change to comply with an update of the relevant monograph of the Ph. Eur. or national pharmacopoeia of a Member State</p>				
WS/1965/G	<p>This was an application for a group of variations following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.</p> <p>C.I.4 (type II): Update of section 5.1 of the SmPC in order to describe the persistence of anti-HBs antibodies in subjects 6 years of age having received a hexavalent vaccine based on the final results from study A3L00052; this is a phase IV, open-label, multi-centre study in children previously vaccinated in Study A3L38a with 3 doses of either Hexacima/Hexyon (Group 1) or Infanrix Hexa (Group 2).</p> <p>C.I.4 (type II): Update of sections 4.4 and 5.1 of the SmPC in order to reword safety and immunogenicity information regarding individuals with immunodeficiency based on the final results from study A3L44; this is a Phase III, single centre, open-label, two-arm study including HIV-exposed infected and uninfected infants vaccinated with a</p>	18/02/2021	28/06/2021	SmPC and PL	<p>The persistence of the immune responses against the hepatitis B component of Hexyon/Hexacima was evaluated in infants. For a 2-dose primary infant series at 3 and 5 months of age without hepatitis B at birth, followed by a toddler booster at 11-12 months of age, 53.8% of children were seroprotected (anti-HBsAg <math>\geq</math> 10 mIU/mL) at 6 years of age, and 96.7% presented an anamnestic response after a challenge dose with a standalone Hepatitis B vaccine. These data support persisting immune memory induced in infants primed with Hexyon/Hexacima.</p> <p>Immunogenicity data in HIV-exposed infants (infected and uninfected) showed that Hexyon//Hexacima is immunogenic in the potentially immunodeficient population of HIV-exposed infants whatever their HIV status at birth. No specific safety concern was observed in this population.</p> <p>Inclusion of syncope within the precautions for use. Syncope can occur following, or even before, any vaccination as a psychogenic response to the needle injection. Procedures should be in place to prevent falling and injury and to</p>

	<p>3-dose infant primary series (at 6, 10, and 14 weeks of age) and a booster dose (at 15 to 18 months of age) with Hexacima/Hexyon in Republic of South Africa. The updates to the SmPC were requested following assessment of these data by Article 46, EMEA/H/C/002702/P46/036 (Hexacima) and EMEA/H/C/002796/P46/034 (Hexyon).</p> <p>C.I.z (type IB): Updated of section 4.4 of the SmPC in order to include syncope within the precautions for use. The package leaflet is updated accordingly. In addition, the WSA took the opportunity to update the list of local representatives in the Package Leaflet.</p> <p>In addition, the WSA took the opportunity to update the product information according to QRD-template 10.1.</p> <p>The RMP version 13.0 has also been submitted.</p> <p>C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data</p> <p>C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data</p> <p>C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation</p>				<p>manage syncope.</p> <p>For more information, please refer to the Summary of Product Characteristics.</p>
WS/1991	This was an application for a variation following a worksharing procedure according to Article 20 of	11/02/2021	n/a		

	<p>Commission Regulation (EC) No 1234/2008.</p> <p>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</p>				
WS/1957/G	<p>This was an application for a group of variations following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.</p> <p>B.I.b.1.a - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Tightening of specification limits for medicinal products subject to OCABR</p> <p>B.I.b.1.c - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Addition of a new specification parameter to the specification with its corresponding test method</p> <p>B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure</p>	21/01/2021	n/a		
WS/1959	<p>This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.</p> <p>B.II.b.2.b - Change to importer, batch release</p>	14/01/2021	n/a		

	arrangements and quality control testing of the FP - Replacement/addition of a site where batch control/testing takes place for a biol/immunol product and any of the test methods at the site is a biol/immunol method				
WS/1906/G	<p>This was an application for a group of variations following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.</p> <p>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</p> <p>B.I.a.4.z - Change to in-process tests or limits applied during the manufacture of the AS - Other variation</p>	10/12/2020	n/a		
WS/1904/G	<p>This was an application for a group of variations following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.</p> <p>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</p> <p>B.I.a.3.c - Change in batch size (including batch size ranges) of AS or intermediate - The change requires assessment of the comparability of a biological/immunological AS</p>	15/10/2020	n/a		

	<p>B.I.a.4.z - Change to in-process tests or limits applied during the manufacture of the AS - Other variation</p> <p>B.III.1.b.2 - Submission of a new/updated or deletion of Ph. Eur. TSE Certificate of Suitability - New certificate for a starting material/reagent/intermediate/or excipient from a new or an already approved manufacturer</p> <p>B.III.1.b.3 - Submission of a new/updated or deletion of Ph. Eur. TSE Certificate of Suitability - Updated certificate from an already approved manufacturer</p>				
WS/1792/G	<p>This was an application for a group of variations following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.</p> <p>C.I.4 (type II) - Update of sections 4.4 and 5.1 of the SmPC in order to revise the warning regarding preterm infants and to add new information on immunogenicity in preterm infants and in infants born from women vaccinated during pregnancy, based on the final results from study A3L00053-EXT; this is an observational cohort study conducted by the Center for the Evaluation of Vaccination in Vaccine and Infectious Diseases Institute of University of Antwerp with DTaP-IPV-HB-PRP~T vaccine, aimed to describe the concentrations of IgG against the different antigens. The RMP version 12.0 has been submitted and updated accordingly, following revision 2 with consequential update to the safety concerns.</p> <p>C.I.z (type IB) - Update of sections 2 and 4.4 of the</p>	24/09/2020	28/06/2021	SmPC and PL	<p>Based on data generated from study A3L00053-EXT, immunogenicity data have been made available for 105 preterm infants (born after a gestation period of 28 to 36 weeks). These data support the use of Hexacima/Hexaxim/Hexyon in preterm infants. As expected in preterm infants, lower immune response has been observed for some antigens, when indirectly compared to term infants, although seroprotective levels have been achieved. Immune responses to Hexacima/Hexaxim/Hexyon in infants born (preterm and term) to women vaccinated with Tdap (tetanus, diphtheria and acellular pertussis) during pregnancy were included in the product information. The rate of seroprotected prior to their own primary vaccination is lower in the pre-term born. Nevertheless, a benefit of the maternal immunization is seen for both groups. The data shown for the Pertussis antigens show that the maternal immunization results in higher geometric mean concentrations (GMCs) in the infants regardless of pre-term status and after the primary and booster immunization all GMCs are similar regardless of vaccination group. The fold</p>

	<p>SmPC in order to add warning for excipients with known effect: phenylalanine, potassium and sodium, according to the European guideline "Excipients in the labeling and package leaflet of medicinal products for human use SANTE-2017-11668". The package leaflet is updated accordingly.</p> <p>In addition, the MAH/SOH took the opportunity to introduce editorial changes in sections 4.2, 4.4, 4.5 and 4.8 of the SmPC and to update the list of local representatives in the Package Leaflet.</p> <p>C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data</p>				<p>increases due to primary immunization are lower in the maternally-vaccinated.</p> <p>For more information, please refer to the Summary of Product Characteristics.</p>
WS/1872/G	<p>This was an application for a group of variations following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.</p> <p>B.I.z - Quality change - Active substance - Other variation B.I.a.4.a - Change to in-process tests or limits applied during the manufacture of the AS - Tightening of in-process limits B.I.a.4.b - Change to in-process tests or limits applied during the manufacture of the AS - Addition of a new in-process test and limits B.I.a.4.b - Change to in-process tests or limits applied</p>	17/09/2020	n/a		



	<p>during the manufacture of the AS - Addition of a new in-process test and limits</p> <p>B.I.a.4.b - Change to in-process tests or limits applied during the manufacture of the AS - Addition of a new in-process test and limits</p>				
WS/1784/G	<p>This was an application for a group of variations following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.</p> <p>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</p> <p>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)</p> <p>B.I.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation</p> <p>B.I.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation</p> <p>B.I.a.1.f - Change in the manufacturer of AS or of 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</p>	17/09/2020	n/a		

WS/1797/G	<p>This was an application for a group of variations following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.</p> <p>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</p> <p>B.I.a.4.b - Change to in-process tests or limits applied during the manufacture of the AS - Addition of a new in-process test and limits</p>	03/09/2020	n/a		
WS/1839/G	<p>This was an application for a group of variations following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.</p> <p>A.7 - Administrative change - Deletion of manufacturing sites</p> <p>B.II.b.1.z - Replacement or addition of a manufacturing site for the FP - Other variation</p>	23/07/2020	n/a		
WS/1815/G	<p>This was an application for a group of variations following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.</p> <p>B.I.b.1.b - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Tightening of specification limits</p>	16/07/2020	n/a		

	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				
WS/1802	<p>This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.</p> <p>B.II.d.2.c - Change in test procedure for the finished product - Substantial change to or replacement of a biol/immunol/immunochemical test method or a method using a biol. reagent or replacement of a biol. reference preparation not covered by an approved protocol</p>	16/07/2020	n/a		
WS/1786	<p>This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.</p> <p>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</p>	02/07/2020	n/a		
WS/1821/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.	25/06/2020	28/06/2021	SmPC	

	<p>B.II.d.1.e - Change in the specification parameters and/or limits of the finished product - Change outside the approved specifications limits range</p> <p>B.II.f.1.b.1 - Stability of FP - Extension of the shelf life of the finished product - As packaged for sale (supported by real time data)</p> <p>B.II.f.1.z - Stability of FP - Change in the shelf-life or storage conditions of the finished product - Other variation</p>				
WS/1699	<p>This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.</p> <p>B.II.d.2.d - Change in test procedure for the finished product - Other changes to a test procedure (including replacement or addition)</p>	27/02/2020	n/a		
WS/1744/G	<p>This was an application for a group of variations following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.</p> <p>B.I.z - Quality change - Active substance - Other variation</p> <p>B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS</p> <p>B.I.a.4.a - Change to in-process tests or limits applied during the manufacture of the AS - Tightening of in-process limits</p>	06/02/2020	n/a		

	<p>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</p> <p>B.I.b.1.e - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Deletion of a specification parameter which may have a significant effect on the overall quality of the AS and/or the FP</p> <p>B.I.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation</p> <p>B.III.1.b.4 - Submission of a new/updated or deletion of Ph. Eur. TSE Certificate of Suitability - Deletion of certificates (in case multiple certificates exist per material)</p>				
WS/1728/G	<p>This was an application for a group of variations following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.</p> <p>B.I.z - Quality change - Active substance - Other variation</p> <p>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</p> <p>B.I.b.1.a - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Tightening of specification limits for medicinal products subject to</p>	23/01/2020	n/a		

	<p>OCABR</p> <p>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)</p> <p>B.I.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation</p> <p>B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure</p> <p>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</p>				
PSUSA/10091 /201904	<p>Periodic Safety Update EU Single assessment - diphtheria / tetanus / pertussis antigens (pertussis toxoid, filamentous haemagglutinin) (acellular, component) / hepatitis b (rdna) / poliomyelitis (inactivated) / haemophilus type b conjugate vaccines (adsorbed)</p>	31/10/2019	n/a		PRAC Recommendation - maintenance
WS/1623	<p>This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.</p> <p>B.I.z - Quality change - Active substance - Other variation</p>	18/07/2019	n/a		

WS/1624/G	<p>This was an application for a group of variations following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.</p> <p>B.II.b.3.a - Change in the manufacturing process of the finished or intermediate product - Minor change in the manufacturing process</p> <p>B.III.2.b - Change to comply with Ph. Eur. or with a national pharmacopoeia of a Member State - Change to comply with an update of the relevant monograph of the Ph. Eur. or national pharmacopoeia of a Member State</p>	04/07/2019	n/a		
WS/1592/G	<p>This was an application for a group of variations following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.</p> <p>A.7 - Administrative change - Deletion of manufacturing sites</p> <p>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</p>	14/06/2019	n/a		
WS/1575/G	<p>This was an application for a group of variations following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.</p> <p>B.I.a.1.e - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - The</p>	29/05/2019	n/a		

	change relates to a biological AS or a starting material [-] used in the manufacture of a biological/immunological product B.I.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation				
WS/1574	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.1.c - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Addition of a new specification parameter to the specification with its corresponding test method	26/04/2019	n/a		
WS/1525	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	11/04/2019	n/a		
WS/1496/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.II.d.1.e - Change in the specification parameters	28/03/2019		SmPC, Labelling and PL	



	<p>and/or limits of the finished product - Change outside the approved specifications limits range</p> <p>B.II.d.2.c - Change in test procedure for the finished product - Substantial change to or replacement of a biol/immunol/immunochemical test method or a method using a biol. reagent or replacement of a biol. reference preparation not covered by an approved protocol</p>				
WS/1455/G	<p>This was an application for a group of variations following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.</p> <p>B.I.b.1.c - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Addition of a new specification parameter to the specification with its corresponding test method</p> <p>B.I.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation</p>	17/01/2019	n/a		
WS/1438/G	<p>This was an application for a group of variations following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.</p> <p>B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS</p> <p>B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of</p>	06/12/2018	n/a		

the AS

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.4.b - Change to in-process tests or limits applied during the manufacture of the AS - Addition of a new in-process test and limits

B.I.a.4.b - Change to in-process tests or limits applied during the manufacture of the AS - Addition of a new in-process test and limits

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

B.I.d.1.b.3 - Stability of AS - Change in the storage conditions - Change in storage conditions of the AS

B.III.1.b.3 - Submission of a new/updated or deletion of Ph. Eur. TSE Certificate of Suitability - Updated certificate from an already approved manufacturer

B.III.1.b.3 - Submission of a new/updated or deletion of Ph. Eur. TSE Certificate of Suitability - Updated certificate from an already approved manufacturer

B.III.1.b.4 - Submission of a new/updated or deletion of Ph. Eur. TSE Certificate of Suitability - Deletion of certificates (in case multiple certificates exist per material)

B.III.1.b.4 - Submission of a new/updated or deletion of Ph. Eur. TSE Certificate of Suitability - Deletion of certificates (in case multiple certificates exist per

	material)				
WS/1393/G	<p>This was an application for a group of variations following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.</p> <p>B.I.b.1.b - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Tightening of specification limits</p> <p>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</p>	22/11/2018	n/a		
PSUSA/10091 /201804	<p>Periodic Safety Update EU Single assessment - diphtheria / tetanus / pertussis antigens (pertussis toxoid, filamentous haemagglutinin) (acellular, component) / hepatitis b (rdna) / poliomyelitis (inactivated) / haemophilus type b conjugate vaccines (adsorbed)</p>	31/10/2018	n/a		PRAC Recommendation - maintenance
WS/1394	<p>This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.</p> <p>B.II.d.2.d - Change in test procedure for the finished product - Other changes to a test procedure (including replacement or addition)</p>	27/09/2018	n/a		

WS/1353/G	<p>This was an application for a group of variations following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.</p> <p>B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure</p> <p>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</p>	20/09/2018	n/a		
WS/1350	<p>This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.</p> <p>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</p>	28/06/2018	n/a		
WS/1304	<p>This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.</p> <p>B.I.d.1.z - Stability of AS - Change in the re-test period/storage period or storage conditions - Other variation</p>	19/04/2018	n/a		
WS/1281/G	This was an application for a group of variations	12/04/2018	n/a		

	<p>following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.</p> <p>B.I.z - Quality change - Active substance - Other variation</p> <p>B.I.a.2.b - Changes in the manufacturing process of the AS - Substantial change to the manufacturing process of the AS which may have a significant impact on the quality, safety or efficacy of the medicinal product</p> <p>B.I.a.4.z - Change to in-process tests or limits applied during the manufacture of the AS - Other variation</p> <p>B.I.a.4.z - Change to in-process tests or limits applied during the manufacture of the AS - Other variation</p> <p>B.I.b.1.b - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Tightening of specification limits</p>				
WS/1306	<p>This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.</p> <p>B.II.d.2.d - Change in test procedure for the finished product - Other changes to a test procedure (including replacement or addition)</p>	22/03/2018	n/a		
WS/1303/G	<p>This was an application for a group of variations following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.</p>	22/02/2018	n/a		

	<p>B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS</p> <p>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</p>				
WS/1286	<p>This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.</p> <p>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</p>	01/02/2018	n/a		
WS/1233/G	<p>This was an application for a group of variations following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.</p> <p>B.I.b.1.c - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Addition of a new specification parameter to the specification with its corresponding test method</p> <p>B.I.b.1.c - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Addition of a new</p>	01/02/2018	n/a		

	<p>specification parameter to the specification with its corresponding test method</p> <p>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</p>				
R/0072	Renewal of the marketing authorisation.	09/11/2017	08/01/2018	SmPC and PL	
IG/0869	A.1 - Administrative change - Change in the name and/or address of the MAH	08/12/2017	17/12/2018	SmPC, Annex II, Labelling and PL	
WS/1185/G	<p>This was an application for a group of variations following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.</p> <p>B.I.z - Quality change - Active substance - Other variation</p> <p>B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS</p>	16/11/2017	n/a		
WS/1231	<p>This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.</p> <p>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</p>	02/11/2017	n/a		

	the AS or a starting material/intermediate				
PSUSA/10091 /201704	Periodic Safety Update EU Single assessment - diphtheria / tetanus / pertussis antigens (pertussis toxoid, filamentous haemagglutinin) (acellular, component) / hepatitis b (rdna) / poliomyelitis (inactivated) / haemophilus type b conjugate vaccines (adsorbed)	26/10/2017	n/a		PRAC Recommendation - maintenance
IG/0854/G	<p>This was an application for a group of variations.</p> <p>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)</p> <p>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)</p> <p>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)</p> <p>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)</p>	20/10/2017	n/a		



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)

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<p>of an obsolete parameter)</p> <p>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)</p> <p>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)</p> <p>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)</p> <p>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)</p> <p>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)</p> <p>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)</p> <p>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)</p> <p>B.I.b.1.d - Change in the specification parameters</p>				
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<p>and/or limits of an AS, starting material/intermediate/reagent - Deletion of a non-significant specification parameter (e.g. deletion of an obsolete parameter)</p> <p>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)</p> <p>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)</p> <p>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)</p> <p>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)</p> <p>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)</p> <p>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)</p> <p>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)</p>				
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non-significant specification parameter (e.g. deletion of an obsolete parameter)

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)

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	Member State to the Ph. Eur.				
WS/1192	<p>This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.</p> <p>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)</p>	14/09/2017	n/a		
WS/1081	<p>This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.</p> <p>B.II.d.2.d - Change in test procedure for the finished product - Other changes to a test procedure (including replacement or addition)</p>	20/07/2017	n/a		
WS/1153	<p>This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.</p> <p>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</p>	13/07/2017	n/a		
WS/1122/G	This was an application for a group of variations following a worksharing procedure according to Article	13/07/2017	n/a		

	<p>20 of Commission Regulation (EC) No 1234/2008.</p> <p>B.I.a.2.z - Changes in the manufacturing process of the AS - Other variation</p> <p>B.I.a.4.a - Change to in-process tests or limits applied during the manufacture of the AS - Tightening of in-process limits</p>				
WS/1174	<p>This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.</p> <p>B.II.d.1.z - Change in the specification parameters and/or limits of the finished product - Other variation</p>	09/06/2017	n/a		
WS/1112	<p>This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.</p> <p>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</p>	01/06/2017	n/a		
IG/0803	A.5.b - Administrative change - Change in the name and/or address of a manufacturer/importer of the finished product, including quality control sites (excluding manufacturer for batch release)	17/05/2017	n/a		
WS/1129/G	This was an application for a group of variations following a worksharing procedure according to Article	11/05/2017	n/a		



	<p>20 of Commission Regulation (EC) No 1234/2008.</p> <p>B.I.b.2.z - Change in test procedure for AS or starting material/reagent/intermediate - Other variation</p> <p>B.I.d.1.z - Stability of AS - Change in the re-test period/storage period or storage conditions - Other variation</p>				
WS/1148/G	<p>This was an application for a group of variations following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.</p> <p>C.I.3.z – To include the information about sequential schedule of hexavalent and pentavalent vaccines in primary series in section 4.2 of SmPC following the assessment of A3L39 study.</p> <p>C.I.4 - Update of section 5.1 of the SmPC in order to include data on persistence of immunity following final results from studies: A3L47: Laboratory analysis on sera stored at Sanofi Pasteur Global Clinical Immunology laboratory and collected within the context of trial PNA19 and A3L49: Phase III, multi-center study in children vaccinated with Hep B vaccine at birth followed by three infant primary series doses of Hexaxim® or Infanrix® hexa in A3L12 study in Thailand</p> <p>C.I.3.z - Change(s) in the SPC, Labelling or PL intended to implement the outcome of a procedure concerning PSUR or PASS or the outcome of the assessment done under A 45/46 - Other variation</p>	21/04/2017	08/01/2018	SmPC	<p>Section 4.2 of SmPC has been amended to include the information on sequential schedule of hexavalent and pentavalent vaccines in primary series: 'When a dose of hepatitis B vaccine is given at birth, the sequential infant primary vaccination hexavalent/pentavalent/hexavalent schedule with Hexaxim/Hexyon/Hexacima and a pentavalent DTaP-IPV/Hib vaccine can be used in accordance with official recommendations.'</p> <p>Section 5.2 has been updated to include information on Persistence of immune response please see the SmPC for details.</p>

	C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				
WS/1146	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.  B.II.f.1.z - Stability of FP - Change in the shelf-life or storage conditions of the finished product - Other variation	21/04/2017	08/01/2018	SmPC	
WS/1071	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.1.a - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Tightening of specification limits for medicinal products subject to OCABR	19/01/2017	n/a		
N/0060	Update of the package leaflets with revised contact details of the local representatives for BE, BG, LU, DA, DE, NL, NO, EL, AT, ES, FR, PT, IE, IS, IT, FI, SE, and UK.  Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	03/01/2017	08/01/2018	PL	
WS/0922/G	This was an application for a group of variations	15/12/2016	n/a		

	<p>following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.</p> <p>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</p> <p>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</p> <p>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</p> <p>B.I.a.2.z - Changes in the manufacturing process of the AS - Other variation</p> <p>B.I.a.4.z - Change to in-process tests or limits applied during the manufacture of the AS - Other variation</p> <p>B.I.b.1.b - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Tightening of specification limits</p> <p>B.I.b.2.z - Change in test procedure for AS or starting material/reagent/intermediate - Other variation</p>				
T/0057	Application for Transfer of Marketing Authorisation from Sanofi Pasteur MSD SNC to Sanofi Pasteur	17/10/2016	11/11/2016	SmPC, Labelling and	

	Europe.  Transfer of Marketing Authorisation			PL	
WS/0964/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.d.2.c - Change in test procedure for the finished product - Substantial change to or replacement of a biol/immunol/immunochemical test method or a method using a biol. reagent or replacement of a biol. reference preparation not covered by an approved protocol	10/11/2016	n/a		
PSUSA/10091 /201604	Periodic Safety Update EU Single assessment - diphtheria / tetanus / pertussis antigens (pertussis toxoid, filamentous haemagglutinin) (acellular, component) / hepatitis b (rdna) / poliomyelitis (inactivated) / haemophilus type b conjugate vaccines (adsorbed)	27/10/2016	n/a		PRAC Recommendation - maintenance
WS/0967	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.	13/10/2016	n/a		

	B.II.d.2.c - Change in test procedure for the finished product - Substantial change to or replacement of a biol/immunol/immunochemical test method or a method using a biol. reagent or replacement of a biol. reference preparation not covered by an approved protocol				
IA/0056/G	This was an application for a group of variations.  A.5.b - Administrative change - Change in the name and/or address of a manufacturer/importer of the finished product, including quality control sites (excluding manufacturer for batch release) A.5.b - Administrative change - Change in the name and/or address of a manufacturer/importer of the finished product, including quality control sites (excluding manufacturer for batch release)	20/09/2016	n/a		
WS/0918/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.d.2.c - Change in test procedure for the finished product - Substantial change to or replacement of a	15/09/2016	n/a		

	biol/immunol/immunochemical test method or a method using a biol. reagent or replacement of a biol. reference preparation not covered by an approved protocol				
WS/0838/G	<p>This was an application for a group of variations following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.</p> <p>B.I.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation</p> <p>B.I.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation</p> <p>B.I.d.1.z - Stability of AS - Change in the re-test period/storage period or storage conditions - Other variation</p>	04/08/2016	n/a		
WS/0913/G	<p>This was an application for a group of variations following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.</p> <p>B.I.z - Quality change - Active substance - Other variation</p> <p>B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure</p> <p>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</p>	19/05/2016	n/a		

	the AS or a starting material/intermediate				
WS/0912/G	<p>This was an application for a group of variations following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.</p> <p>B.I.b.1.e - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Deletion of a specification parameter which may have a significant effect on the overall quality of the AS and/or the FP</p> <p>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</p> <p>B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure</p> <p>B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure</p> <p>B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure</p> <p>B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure</p> <p>B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure</p> <p>B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure</p>	12/05/2016	n/a		

	<p>material/reagent/intermediate - Minor changes to an approved test procedure</p> <p>B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure</p>				
WS/0907	<p>This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.</p> <p>C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data</p>	28/04/2016	11/11/2016	SmPC	
WS/0901/G	<p>This was an application for a group of variations following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.</p> <p>B.I.a.2.b - Changes in the manufacturing process of the AS - Substantial change to the manufacturing process of the AS which may have a significant impact on the quality, safety or efficacy of the medicinal product</p> <p>B.I.d.z - Stability of AS - Other variation</p>	14/04/2016	n/a		
WS/0885	<p>This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.</p> <p>B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an</p>	07/04/2016	n/a		



	approved test procedure				
WS/0874	<p>This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.</p> <p>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</p>	01/04/2016	n/a		
WS/0853	<p>This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.</p> <p>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</p>	11/02/2016	n/a		
WS/0869	<p>This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.</p> <p>B.II.e.1.a.3 - Change in immediate packaging of the finished product - Qualitative and quantitative composition - Sterile medicinal products and biological/immunological medicinal products</p>	14/01/2016	n/a		
WS/0832/G	This was an application for a group of variations following a worksharing procedure according to Article	10/12/2015	n/a		

	<p>20 of Commission Regulation (EC) No 1234/2008.</p> <p>B.I.z - Quality change - Active substance - Other variation</p> <p>B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure</p>				
WS/0797/G	<p>This was an application for a group of variations following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.</p> <p>B.I.z - Quality change - Active substance - Other variation</p> <p>B.III.1.b.3 - Submission of a new/updated or deletion of Ph. Eur. TSE Certificate of Suitability - Updated certificate from an already approved manufacturer</p>	03/12/2015	n/a		
WS/0842	<p>This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.</p> <p>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</p>	26/11/2015	n/a		
WS/0789	<p>This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.</p>	19/11/2015	20/05/2016	SmPC and PL	This variation application has been submitted in order to include 'convulsions with or without fever' and 'anaphylactic reactions' for the DTaP-IPV-HB-PRP-T hexavalent vaccine

	<p>Update of section 4.8 of the SmPC, upon request by PRAC following the assessment of PSUSA/10091/201410, to include 'convulsion with or without fever' and 'anaphylactic reaction' as ADRs. The Package Leaflet has been updated accordingly. In addition, for Hexyon the WSA took the opportunity to update the contact details for the local representative in Romania in the Package Leaflet. An updated RMP version 10.0 was agreed during the procedure.</p> <p>C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data</p>				(Hexyon, Hexacima, Hexaxim) as adverse reactions reported during commercial use in section 4.8 of the SmPC with a frequency classification of 'rare'. 'Convulsions with or without fever' and 'anaphylactic reactions' were already listed in section 4.8 of the SmPC as potential adverse events (i.e. adverse events which have been reported with other vaccines).
IG/0625	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	16/11/2015	n/a		
PSUSA/10091 /201504	Periodic Safety Update EU Single assessment - diphtheria / tetanus / pertussis antigens (pertussis toxoid, filamentous haemagglutinin) (acellular, component) / hepatitis b (rdna) / poliomyelitis (inactivated) / haemophilus type b conjugate vaccines (adsorbed)	06/11/2015	n/a		PRAC Recommendation - maintenance
WS/0796	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.	01/10/2015	n/a		

	B.III.2.a.2 - Change of specification(s) of a former non EU Pharmacopoeial substance to fully comply with the Ph. Eur. or with a national pharmacopoeia of a Member State - Excipient/AS starting material				
IA/0037	B.II.b.3.a - Change in the manufacturing process of the finished or intermediate product - Minor change in the manufacturing process	23/09/2015	n/a		
WS/0773	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	17/09/2015	n/a		
WS/0729	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.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	17/09/2015	n/a		
IA/0033	B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an	16/07/2015	n/a		

	approved test procedure				
IA/0032/G	<p>This was an application for a group of variations.</p> <p>B.II.c.1.b - Change in the specification parameters and/or limits of an excipient - Addition of a new specification parameter to the specification with its corresponding test method</p> <p>B.II.c.1.b - Change in the specification parameters and/or limits of an excipient - Addition of a new specification parameter to the specification with its corresponding test method</p>	29/06/2015	n/a		
WS/0568/G	<p>This was an application for a group of variations following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.</p> <p>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</p> <p>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</p> <p>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</p> <p>B.I.a.4.b - Change to in-process tests or limits applied</p>	25/06/2015	n/a		

	<p>during the manufacture of the AS - Addition of a new in-process test and limits</p> <p>B.I.a.4.b - Change to in-process tests or limits applied during the manufacture of the AS - Addition of a new in-process test and limits</p> <p>B.I.a.4.b - Change to in-process tests or limits applied during the manufacture of the AS - Addition of a new in-process test and limits</p> <p>B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS</p>				
WS/0749/G	<p>This was an application for a group of variations following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.</p> <p>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</p> <p>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</p> <p>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</p>	04/06/2015	n/a		

	biological AS				
N/0030	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	26/05/2015	20/05/2016	PL	
IA/0028	B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure	21/05/2015	n/a		
WS/0702	<p>This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.</p> <p>Update of sections 4.5 and 5.1 of the SmPC in order to add the information on co-administration of the hexavalent vaccine with meningococcal serogroup C vaccine. The Package Leaflet is updated accordingly. The MAH took also the opportunity to make minor editorial changes throughout the PI.</p> <p>C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data</p>	21/05/2015	20/05/2016	SmPC and PL	In this variation the Product information has been updated with the information that co-administration of the hexavalent vaccine with meningococcal serogroup C vaccine does not lead to any clinically relevant interference in the antibody response to each of the antigens.
IA/0029	B.III.1.b.3 - Submission of a new/updated or deletion of Ph. Eur. TSE Certificate of Suitability - Updated certificate from an already approved manufacturer	18/05/2015	n/a		
IA/0027	B.I.b.1.b - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Tightening of	13/05/2015	n/a		

	specification limits				
PSUSA/10091 /201410	Periodic Safety Update EU Single assessment - diphtheria / tetanus / pertussis antigens (pertussis toxoid, filamentous haemagglutinin) (acellular, component) / hepatitis b (rdna) / poliomyelitis (inactivated) / haemophilus type b conjugate vaccines (adsorbed)	07/05/2015	n/a		PRAC Recommendation - maintenance
WS/0727/G	<p>This was an application for a group of variations following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.</p> <p>A.5.b - Administrative change - Change in the name and/or address of a manufacturer/importer of the finished product, including quality control sites (excluding manufacturer for batch release)</p> <p>B.II.b.2.a - Change to importer, batch release arrangements and quality control testing of the FP - Replacement/addition of a site where batch control/testing takes place</p>	23/04/2015	n/a		
WS/0678/G	<p>This was an application for a group of variations following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.</p> <p>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</p>	26/03/2015	n/a		



	<p>biological AS</p> <p>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</p>				
WS/0677	<p>This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.</p> <p>B.II.d.2.c - Change in test procedure for the finished product - Substantial change to or replacement of a biol/immunol/immunochemical test method or a method using a biol. reagent or replacement of a biol. reference preparation not covered by an approved protocol</p>	26/02/2015	n/a		
WS/0676	<p>This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.</p> <p>Update of sections 4.2 and 5.1 of the SmPC with regards to 2+1 vaccination schedule combining a 2 dose priming series with a booster vaccination, further to the results of Phase III Study A3L38 conducted in healthy infants and toddlers (MEA 005). The package leaflet is updated accordingly. The MAH has taken also the opportunity to revise information of the local representative for Croatia in Hexacima PL, and to</p>	22/01/2015	24/02/2015	SmPC and PL	<p>Analysis of data provided in study A3L38 confirm that administration of two doses (with an interval of at least 8 weeks) or three doses (with an interval of at least 4 weeks), in accordance with the official recommendations, together with one booster dose are capable of providing an adequate antibody response against each valence. No new safety concern with Hexacima/Hexyon administered in a 2+1 schedule emerged during the course of study A3L38.</p>

	<p>bring in line the PL for Hexaxim with the latest QRD v.9.0.</p> <p>C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data</p>				
IB/0020/G	<p>This was an application for a group of variations.</p> <p>B.II.e.5.a.2 - Change in pack size of the finished product - Change in the number of units (e.g. tablets, ampoules, etc.) in a pack - Change outside the range of the currently approved pack sizes</p> <p>B.II.e.5.a.2 - Change in pack size of the finished product - Change in the number of units (e.g. tablets, ampoules, etc.) in a pack - Change outside the range of the currently approved pack sizes</p>	07/01/2015	24/02/2015	SmPC, Labelling and PL	
WS/0652/G	<p>This was an application for a group of variations following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.</p> <p>Changes to the manufacturing process of the active substance (IPV)</p> <p>B.I.a.3.c - Change in batch size (including batch size ranges) of AS or intermediate - The change requires assessment of the comparability of a biological/immunological AS</p> <p>B.I.a.2.c - Changes in the manufacturing process of the AS - The change refers to a [-] substance in the</p>	18/12/2014	n/a		

	<p>manufacture of a biological/immunological substance which may have a significant impact on the medicinal product and is not related to a protocol</p> <p>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</p> <p>B.I.b.1.c - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Addition of a new specification parameter to the specification with its corresponding test method</p> <p>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)</p>				
WS/0594/G	<p>This was an application for a group of variations following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.</p> <p>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</p> <p>B.III.2.b - Change to comply with Ph. Eur. or with a national pharmacopoeia of a Member State - Change to comply with an update of the relevant monograph of the Ph. Eur. or national pharmacopoeia of a Member</p>	18/12/2014	n/a		

	<p>State</p> <p>B.III.2.b - Change to comply with Ph. Eur. or with a national pharmacopoeia of a Member State - Change to comply with an update of the relevant monograph of the Ph. Eur. or national pharmacopoeia of a Member State</p>				
WS/0617/G	<p>This was an application for a group of variations following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.</p> <p>B.I.a.1.e - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - The change relates to a biological AS or a starting material [-] used in the manufacture of a biological/immunological product</p> <p>B.I.a.1.f - Change in the manufacturer of AS or of 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</p>	20/11/2014	n/a		
PSUV/0013	Periodic Safety Update	06/11/2014	n/a		PRAC Recommendation - maintenance
WS/0580	<p>This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.</p> <p>changes to the manufacturing process of the active substance</p>	24/07/2014	n/a		

	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				
IAIN/0011	B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site	14/05/2014	n/a		
IAIN/0010	A.1 - Administrative change - Change in the name and/or address of the MAH	08/05/2014	27/10/2014	SmPC, Labelling and PL	
PSUV/0006	Periodic Safety Update	08/05/2014	n/a		PRAC Recommendation - maintenance
WS/0547	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.  Change in test procedures for the active substance.  B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure	25/04/2014	n/a		
IG/0434	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	09/04/2014	n/a		

IB/0007	B.I.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation	04/04/2014	n/a		
PSUV/0003	Periodic Safety Update	09/01/2014	n/a		PRAC Recommendation - maintenance
IA/0005	B.III.2.b - Change to comply with Ph. Eur. or with a national pharmacopoeia of a Member State - Change to comply with an update of the relevant monograph of the Ph. Eur. or national pharmacopoeia of a Member State	13/11/2013	n/a		
IAIN/0004	C.I.12 - Inclusion or deletion of black symbol and explanatory statements for medicinal products in the list of medicinal products that are subject to additional monitoring	11/11/2013	27/10/2014	SmPC and PL	
WS/0462/G	<p>This was an application for a group of variations following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.</p> <p>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</p> <p>B.I.b.1.b - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Tightening of specification limits</p> <p>B.I.a.2.c - Changes in the manufacturing process of</p>	24/10/2013	n/a		

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.b.1.b - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Tightening of specification limits

B.I.b.1.h - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Addition or replacement (excl. Biol. or immunol. substance) of a specification parameter as a result of a safety or quality issue

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.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.b.1.b - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Tightening of specification limits

B.III.1.b.3 - Submission of a new/updated or deletion of Ph. Eur. TSE Certificate of Suitability - Updated certificate from an already approved manufacturer

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.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.d.1.a.3 - Stability of AS - Change in the re-test period/storage period - Extension of storage period of a biological/immunological AS not in accordance with an approved stability protocol

B.I.a.4.b - Change to in-process tests or limits applied during the manufacture of the AS - Addition of a new in-process test and limits

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.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.1.e - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - The change relates to a biological AS or a starting material [-] used in the manufacture of a biological/immunological product

B.I.b.1.z - Change in the specification parameters and/or limits of an AS, starting



	<p>material/intermediate/reagent - Other variation</p> <p>B.I.b.1.b - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Tightening of specification limits</p> <p>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</p> <p>B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure</p> <p>B.II.d.2.d - Change in test procedure for the finished product - Other changes to a test procedure (including replacement or addition)</p> <p>B.II.c.3.z - Change in source of an excipient or reagent with TSE risk - Other variation</p>				
WS/0431/G	<p>This was an application for a group of variations following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.</p> <p>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.</p> <p>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.</p>	19/09/2013	n/a		

