Gardasil 9

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
IAIN/0076	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	09/10/2024		SmPC and PL	
II/0074	B.II.b.5.e - Change to in-process tests or limits applied during the manufacture of the finished product - Widening of the approved IPC limits, which	19/09/2024	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).

	may have a significant effect on overall quality of the finished product				
IB/0075/G	This was an application for a group of variations. 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.a.1.z - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Other variation	09/07/2024	n/a		
IA/0073	B.I.b.2.b - Change in test procedure for AS or starting material/reagent/intermediate - Deletion of a test procedure for the AS or a starting material/reagent/intermediate, if an alternative test procedure is already authorised	09/05/2024	n/a		
IB/0072	B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS	26/03/2024	n/a		
IB/0071/G	This was an application for a group of variations. 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 B.I.e.5.c - Implementation of changes foreseen in an	26/03/2024		Annex II	

	approved change management protocol - For a biological/immunological medicinal product				
II/0069	C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	21/03/2024		SmPC and PL	Gardasil SmPC section 5.1 has been modified to include updated information on long term-effectiveness. The numbers on years pot-dose, median follow-up years and number of people followed have been updated.
IB/0070	B.II.b.1.z - Replacement or addition of a manufacturing site for the FP - Other variation	05/01/2024	n/a		
IB/0068	B.II.b.1.z - Replacement or addition of a manufacturing site for the FP - Other variation	22/08/2023	n/a		
IB/0067	B.II.d.2.d - Change in test procedure for the finished product - Other changes to a test procedure (including replacement or addition)	20/06/2023	n/a		
IB/0066	B.II.g.5.c - Implementation of changes foreseen in an approved change management protocol - For a biological/immunological medicinal product	19/06/2023	n/a		
II/0063	Update of section 4.6 of the SmPC in order to include additional information on exposure during pregnancy based on the final report of the US Pregnancy Registry, listed as a category 3 study in the RMP (MEA 003.1 is fulfilled with this procedure). The Package Leaflet is updated accordingly. The RMP version 5.1 has been approved with this procedure. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance	12/05/2023		SmPC and PL	The SmPC text Section 4.6 has been updated to include the results of the pregnancy registry. The recommendation to avoid Gardasil 9 in case of pregnancy is maintained. The Package leaflet was updated accordingly to specify that if a woman is pregnant or becomes pregnant during the course of vaccination, it is recommended to postpone or interrupt vaccination until they are no longer pregnant.

	data				
PSUSA/10389 /202206	Periodic Safety Update EU Single assessment - human papillomavirus 9-valent vaccine (recombinant, adsorbed)	26/01/2023	31/03/2023	SmPC	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/10389/202206.
IB/0064	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	23/01/2023	n/a		
II/0061	B.II.g.2 - Introduction of a post approval change management protocol related to the finished product	15/12/2022	n/a		
II/0060/G	This was an application for a group of variations. B.II.b.1.c - Replacement or addition of a manufacturing site for the FP - Site where any manufacturing operation(s) take place, except batch release/control, and secondary packaging, for biol/immunol medicinal products or pharmaceutical forms manufactured by complex manufacturing processes B.II.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 B.II.e.4.c - Change in shape or dimensions of the container or closure (immediate packaging) - Sterile medicinal products	01/12/2022	n/a		

IB/0062	B.II.g.5.c - Implementation of changes foreseen in an approved change management protocol - For a biological/immunological medicinal product	18/11/2022	n/a		
WS/2336	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. Update of section 5.1 of the SmPC to add the effect of vaccination campaigns on the reduction in the incidence of Juvenile-onset Recurrent Respiratory Papillomatosis (JoRRP) based upon published observational studies. In addition, the MAH took the opportunity to introduce minor editorial changes to the SmPC. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	13/10/2022	31/03/2023	SmPC	The following wording about the effect of vaccination campaigns on the reduction in the incidence of Juvenile-onset Recurrent Respiratory Papillomatosis (JoRRP) based upon published observational studies was agreed for addition to SmPC section 5.1: "JoRRP is caused by upper airway infection primarily with HPV types 6 and 11, acquired vertically (mother-to-child) during childbirth. Observational studies in the US and Australia have shown that the introduction of Gardasil since 2006 has led to declines in the incidence of JoRRP at population level."
IG/1529/G	This was an application for a group of variations. A.4 - Administrative change - Change in the name and/or address of a manufacturer or an ASMF holder or supplier of the AS, starting material, reagent or intermediate used in the manufacture of the AS or manufacturer of a novel excipient A.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.4 - Administrative change - Change in the name	06/07/2022	31/03/2023	Annex II	

	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				
IB/0055	B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS	10/06/2022	n/a		
IB/0056	B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS	09/06/2022	n/a		
T/0054	Transfer of Marketing Authorisation	14/03/2022	29/04/2022	SmPC, Labelling and PL	
II/0053	Update of section 5.1 of the SmPC in order to update long-term effectiveness and immunogenicity data following the final results of the Gardasil 9 long-term follow-up (LTFU) paediatric study V503-002-20, listed as a category 3 study in the RMP. V503-002-20 is a LTFU extension of Study V503-002 (base study: a 3-year immunogenicity study of the 9vHPV vaccine in girls and boys 9 to 15 years of age, which assessed the immunogenicity and effectiveness of the 9vHPV vaccine through 10 years post dose 3. In addition, the MAH took the opportunity to make some minor editorial changes (spacings) and included the updated long term follow-up data already approved for the qHPV vaccine following V501-167 extension study. The details of local	24/03/2022	31/03/2023	SmPC and PL	Please refer to Scientific Discussion EMEA/H/C/003852/II/0053 For more information, please refer to the Summary of Product Characteristics

	representatives for the MAH in the Package Leaflet is also updated. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				
PSUSA/10389 /202106	Periodic Safety Update EU Single assessment - human papillomavirus 9-valent vaccine (recombinant, adsorbed)	13/01/2022	n/a		PRAC Recommendation - maintenance
IB/0052	B.II.f.1.d - Stability of FP - Change in storage conditions of the finished product or the diluted/reconstituted product	10/11/2021	28/04/2022	SmPC and PL	
IB/0048/G	This was an application for a group of variations. B.I.a.2.z - Changes in the manufacturing process of the AS - Other variation B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure	15/10/2021	n/a		
IB/0051	C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation	13/10/2021	n/a		
IB/0047	B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS	05/10/2021	n/a		

II/0046	B.II.g.2 - Introduction of a post approval change management protocol related to the finished product	16/09/2021	n/a		
IA/0049	B.II.e.7.b - Change in supplier of packaging components or devices (when mentioned in the dossier) - Replacement or addition of a supplier	10/08/2021	n/a		
WS/2037	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. B.I.e.2 - Introduction of a post approval change management protocol related to the AS	24/06/2021	n/a		
II/0044	B.II.b.2.b - Change to importer, batch release 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	28/01/2021	n/a		
PSUSA/10389 /202006	Periodic Safety Update EU Single assessment - human papillomavirus 9-valent vaccine (recombinant, adsorbed)	14/01/2021	n/a		PRAC Recommendation - maintenance
II/0040	C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	14/01/2021	28/04/2022	SmPC and PL	
II/0043/G	This was an application for a group of variations. B.I.a.2.c - Changes in the manufacturing process of	29/10/2020	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.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				
IB/0041/G	This was an application for a group of variations. B.II.b.1.z - Replacement or addition of a manufacturing site for the FP - Other variation B.II.b.5.z - Change to in-process tests or limits applied during the manufacture of the finished product - Other variation B.II.b.5.z - Change to in-process tests or limits applied during the manufacture of the finished product - Other variation	30/07/2020	n/a		
II/0038/G	This was an application for a group of variations. 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 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 B.I.b.1.f - Change in the specification parameters	23/07/2020	n/a		

	and/or limits of an AS, starting material/intermediate/reagent - Change outside the approved specifications limits range for the AS				
IA/0039	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)	29/06/2020	n/a		
II/0037/G	This was an application for a group of variations. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	17/04/2020	24/11/2020	SmPC, Annex II, Labelling and PL	
PSUSA/10389 /201906	Periodic Safety Update EU Single assessment - human papillomavirus 9-valent vaccine (recombinant, adsorbed)	16/01/2020	n/a		PRAC Recommendation - maintenance
R/0035	Renewal of the marketing authorisation.	14/11/2019	16/01/2020	SmPC, Labelling and PL	
II/0033	Update of sections 4.2, 4.6, 4.8 and 5.1 of the SmPC in order to update the safety and immunogenicity information based on final results from study V503-	28/11/2019	24/11/2020	SmPC and PL	

	P004 listed as a category 3 study in the RMP (MEA007); this is an open-label phase III clinical trial to study the immunogenicity and tolerability of Gardasil 9 in adult women (27 to 45 year-olds) compared to young adult women (16 to 26 year-olds); the Package Leaflet is updated accordingly. The RMP version 4.1 has also been submitted. In addition, the Marketing authorisation holder (MAH) took the opportunity to update Section 4.4 of the SmPC according to the Guideline on quality aspects included in the product information for vaccines for human use (EMA/CHMP/BWP/133540/2017), and to include editorial changes in Section 5.1 of the SmPC The requested variation proposed amendments to the Summary of Product Characteristics and Package Leaflet and to the Risk Management Plan (RMP). C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				
IAIN/0034	B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site	14/08/2019	n/a		
PSUSA/10389 /201812	Periodic Safety Update EU Single assessment - human papillomavirus 9-valent vaccine (recombinant, adsorbed)	11/07/2019	n/a		PRAC Recommendation - maintenance
IAIN/0032	B.II.e.5.a.1 - Change in pack size of the finished product - Change in the number of units (e.g.	29/04/2019	25/07/2019	SmPC, Labelling and	

	tablets, ampoules, etc.) in a pack - Change within the range of the currently approved pack sizes			PL	
IB/0031/G	This was an application for a group of variations. B.II.d.1.b - Change in the specification parameters and/or limits of the finished product - Tightening of specification limits for medicinal products subject to OCABR B.II.d.1.d - Change in the specification parameters and/or limits of the finished product - Deletion of a non-significant specification parameter B.II.d.2.b - Change in test procedure for the finished product - Deletion of a test procedure if an alternative method is already authorised	15/04/2019	n/a		
II/0029	C.I.11.b - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Implementation of change(s) which require to be further substantiated by new additional data to be submitted by the MAH where significant assessment is required	14/02/2019	n/a		
II/0028	Update of section 5.1 of the SmPC in order to consolidate the existing information following a request of the CHMP (EMEA/H/C/003852/II/0024/G). In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the Package Leaflet. C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	17/01/2019	25/07/2019	SmPC and PL	

PSUSA/10389 /201806	Periodic Safety Update EU Single assessment - human papillomavirus 9-valent vaccine (recombinant, adsorbed)	17/01/2019	n/a		PRAC Recommendation - maintenance
II/0025	Changes in the manufacturing process of the active substance (Human Papillomavirus 9-valent Vaccine (Recombinant, adsorbed), specifically the HPV 16 L1 protein) to increase the lifetime of filters membranes and chromatography resins. The requested variation proposed no amendments to the Product Information. 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	26/07/2018	n/a		
II/0024/G	This was an application for a group of variations. Update of section 5.1 of the SmPC with information on results from long-term follow-up (LTFU) studies. Specifically: – addition of a long-term effectiveness sub-section, based on the first interim reports from the 9vHPV studies V503-021-01 and V503-002-20 (two category 3 studies included in the pharmacovigilance plan of the 9vHPV vaccine - MEA-004 and MEA 005, respectively), – update of the immunogenicity sub-section based on the data from the two 9vHPV studies listed	26/07/2018	25/07/2019	SmPC	

	above as well as final results from studies V503-001-04 and V503-010-01, – update of the qHPV clinical data based on the efficacy/effectiveness results and/or immunogenicity results of the qHPV studies V501-015-21 (4th interim report), V501-019-21 (final study report), V501-020-21 (final study report) and the extension of study V501-167. The MAH also took the opportunity to introduce minor amendments throughout the product information. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				
IB/0026	B.II.b.3.a - Change in the manufacturing process of the finished or intermediate product - Minor change in the manufacturing process	24/07/2018	n/a		
PSUSA/10389 /201712	Periodic Safety Update EU Single assessment - human papillomavirus 9-valent vaccine (recombinant, adsorbed)	12/07/2018	n/a		PRAC Recommendation - maintenance
PSUSA/10389 /201706	Periodic Safety Update EU Single assessment - human papillomavirus 9-valent vaccine	11/01/2018	n/a		PRAC Recommendation - maintenance

	(recombinant, adsorbed)				
IB/0022	C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation	05/01/2018	n/a		
N/0021	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	27/11/2017	19/02/2018	Labelling and PL	
II/0019/G	This was an application for a group of variations. B.II.b.1.c: To add MSD International GmbH T/A MSD Ireland (Carlow), Dublin Road, Carlow, Co. Carlow, Ireland as an alternative site responsible for final formulated bulk pooling and primary packaging of Gardasil 9 suspension for injection in pre-filled syringes. B.II.b.2.a: To add MSD International GmbH T/A MSD Ireland (Carlow), Dublin Road, Carlow, Co. Carlow, Ireland as an alternative site responsible for batch/control testing for bacterial endotoxin and sterility tests for Gardasil 9 suspension for injection in pre-filled syringes. B.II.b.1.c - Replacement or addition of a manufacturing site for the FP - Site where any manufacturing operation(s) take place, except batch release/control, and secondary packaging, for biol/immunol medicinal products or pharmaceutical forms manufactured by complex manufacturing processes	13/07/2017	n/a		

	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				
PSUSA/10389 /201612	Periodic Safety Update EU Single assessment - human papillomavirus 9-valent vaccine (recombinant, adsorbed)	06/07/2017	n/a		PRAC Recommendation - maintenance
N/0018	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	24/03/2017	19/02/2018	PL	
IG/0777	A.1 - Administrative change - Change in the name and/or address of the MAH	23/02/2017	19/02/2018	SmPC, Labelling and PL	
II/0013	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	19/01/2017	n/a		
PSUSA/10389 /201606	Periodic Safety Update EU Single assessment - human papillomavirus 9-valent vaccine (recombinant, adsorbed)	12/01/2017	n/a		PRAC Recommendation - maintenance
IG/0758	A.1 - Administrative change - Change in the name and/or address of the MAH	11/01/2017	03/03/2017	SmPC, Labelling and PL	
N/0014	Update of the package leaflet with revised contact details of the local representatives.	21/12/2016	03/03/2017	PL	

	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)				
PSUSA/10389 /201512	Periodic Safety Update EU Single assessment - human papillomavirus 9-valent vaccine (recombinant, adsorbed)	07/07/2016	n/a		PRAC Recommendation - maintenance
II/0010	Update of section 5.1 of the SmPC in order to include clinical data based on the final clinical study report for the paediatric study V503-020 (GDS07C), provided as per the requirements of article 46 of the paediatric regulation. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	12/05/2016	03/03/2017	SmPC	Study GDS07C compared immune responses to 9vHPV vaccine with immune responses to 4vHPV vaccine in 16-26 years old boys and men. The responses to the 4 common HPV types (6, 11, 16 and 18) were shown to be non-inferior in the 9vHPV group compared to the 4vHPV group. The responses to the 5 new HPV types were greater in the 9vHPV group compared to the 4 vHPV group. The results were overall in agreement with the results previously shown in women 16-26 years of age. The safety results confirm the safety profile of the 9vHPV vaccine, and non new safety signal was detected.
IB/0011	B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS	26/04/2016	n/a		
II/0004	Update of sections 4.2 and 5.1 of the SmPC in order to add an alternative 2-dose vaccination schedule for children from 9 to 14 years of age based on study results of Protocol V503-010 and section 4.8 of the SmPC in order to add bronchospasm and urticaria. The Package Leaflet is updated accordingly. For clarity, minor amendments have been included in Sections 4.4, and 4.6 and 5.1 of the SmPC. In addition, the Marketing authorisation holder	25/02/2016	04/04/2016	SmPC, Annex II, Labelling and PL	The MAH provided the results of a study V503-010 to investigate an alternative 2-dose vaccination schedule for children from 9 to 14 years of age. Results showed comparable immune responses in 2-dose recipients compared to the 3-dose recipients and support the proposed addition of a 2-dose schedule. For completeness and to align with the SmPC of Gardasil section 4.8 of the SmPC was updated to add bronchospasm and urticaria.

	(MAH) took the opportunity to update the list of local representatives in the Package Leaflet, to bring the PI in line with the latest QRD template version 10 and to combine the SmPCs of the suspension for injection and the suspension for injection in a pre filled syringe. Furthermore, the MAH implemented minor linguistic revisions in the Portuguese, Czeck and Slovak texts. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				
II/0007	Update of section 5.1 of SmPC with the results of 4 long term follow-up studies (final study P018-11 and interim reports for Studies P015-21, P019-21 and P020-21). C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	01/04/2016	03/03/2017	SmPC	Section 5.1 of SmPC was updated with the results of 4 long term follow-up studies in adolescents (final study P018-11 and interim reports for long term follow-up studies in young/mid-adult women and young men (Studies P015-21, P019-21 and P020-21). In the long-term extension registry study for 16-23 year old women vaccinated with qHPV vaccine, a durable protection was statistically demonstrated to approximately 8 years.
IB/0008	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	26/01/2016	n/a		
A20/0001	Pursuant to Article 20 of Regulation (EC) No 726/2004, the European Commission requested on 09 July 2015 the opinion of the European Medicines Agency on whether there is evidence of a causal	19/11/2015	12/01/2016		Please refer to the assessment report: Cervarix: EMEA/H/A20/1421/C/0721/0071 Gardasil: EMEA/H/A20/1421/C/0703/0060 Gardasil 9: EMEA/H/A20/1421/C/3852/0001

	association between HPV vaccination and CRPS and/or POTS, and if available information may require updates to the advice to healthcare professionals and patients, including changes to product information or other regulatory measures on the marketing authorisations concerned. As the request results from the evaluation of data resulting from pharmacovigilance activities, the CHMP opinion should be adopted on the basis of a recommendation of the Pharmacovigilance Risk Assessment Committee.				Silgard: EMEA/H/A20/1421/C/0732/0054
N/0006	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	21/12/2015	04/04/2016	PL	
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		
II/0003	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	15/10/2015	n/a		
II/0002	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	17/09/2015	n/a		

	product and is not related to a protocol				