Shingrix

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
II/0076	Update of sections 4.8 and 5.1 of the SmPC to include the final results of study ZOSTER-049, listed as a category 3 study in the RMP. This is a Phase 3b, open label, multi-country, long-term follow-up study that assessed the prophylactic efficacy, safety, and immunogenicity persistence of Shingrix in adults ≥50	13/03/2025		SmPC, Labelling and PL	The SmPC sections 4.8 and 5.1 of the SmPC have been updated to include information on the final results of study ZOSTER-049 a long-term follow-up study that assessed the prophylactic efficacy, safety, and immunogenicity persistence of Shingrix in adults ≥50 years of age at the time of primary vaccination. The

[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).

	years of age at the time of primary vaccination in studies ZOSTER 006 and ZOSTER-022. The study also assessed 1 or 2 additional doses of Shingrix on a 0 or 0, 2-month schedule in two subgroups of older adults. The updated RMP version 8.2 has been approved. In addition, the MAH took the opportunity to implement editorial changes to the SmPC, Labelling and Package Leaflet; and to bring the PI in line with the latest QRD template version 10.4. Based on this, sections 2, 4.4 and 6.6 of the SmPC have been updated. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				Package Leaflet was updated accordingly. For more information, please refer to the Summary of Product Characteristics.
IAIN/0078	B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site	26/07/2024	n/a		
IB/0077	B.II.b.3.a - Change in the manufacturing process of the finished or intermediate product - Minor change in the manufacturing process	12/07/2024	n/a		
PSUSA/10678 /202310	Periodic Safety Update EU Single assessment - herpes zoster vaccine (recombinant, adjuvanted)	16/05/2024	n/a		PRAC Recommendation - maintenance
IB/0075	B.II.b.3.a - Change in the manufacturing process of the finished or intermediate product - Minor change in the manufacturing process	27/02/2024	n/a		

IB/0074	B.II.g.5.c - Implementation of changes foreseen in an approved change management protocol - For a biological/immunological medicinal product	27/02/2024	n/a		
WS/2585	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. B.II.c.4.c - Change in synthesis or recovery of a non-pharmacopoeial or novel excipient excipient - The excipient is a biological/immunological substance	01/02/2024	n/a		
IG/1677	B.III.2.z - Change to comply with Ph. Eur. or with a national pharmacopoeia of a Member State - Other variation	27/11/2023	n/a		
II/0069	B.II.g.2 - Introduction of a post approval change management protocol related to the finished product	16/11/2023	n/a		
II/0068	B.I.e.2 - Introduction of a post approval change management protocol related to the AS	09/11/2023	n/a		
IB/0070/G	This was an application for a group of variations. B.II.b.3.z - Change in the manufacturing process of the finished or intermediate product - Other variation B.II.b.4.z - Change in the batch size (including batch size ranges) of the finished product - Other variation	27/10/2023	n/a		
II/0065	Update of section 4.5 of the SmPC in order to add drug-drug interaction information with COVID-19 mRNA-1273 booster vaccine, based on final results	26/10/2023	27/09/2024	SmPC and PL	The SmPC section 4.5 has been updated to include information on the co-administration of Shingrix with coronavirus disease 2019 (COVID-19) messenger

	from study ZOSTER-091; this is a phase 3, randomized, open-label, controlled, multi-center clinical study to evaluate the immune response and safety of both herpes zoster subunit vaccine (HZ/su or Shingrix) in healthy adults aged 50 years and older, and the quadrivalent seasonal influenza vaccine (Flu D-QIV or Fluarix Quadrivalent) in healthy adults aged 18 years and older, when administered sequentially or co-administered with mRNA-1273 booster vaccination. The Package Leaflet is updated accordingly. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				ribonucleic acid (mRNA) vaccine. The Package Leaflet was updated accordingly. For more information, please refer to the Summary of Product Characteristics.
IB/0067	B.II.e.3.z - Change in test procedure for the immediate packaging of the finished product - Other variation	26/07/2023	n/a		
WS/2471/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.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 B.I.b.2.d - Change in test procedure for AS or	13/07/2023	n/a		

	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				
PSUSA/10678 /202210	Periodic Safety Update EU Single assessment - herpes zoster vaccine (recombinant, adjuvanted)	12/05/2023	n/a		PRAC Recommendation - maintenance
IB/0063	B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS	20/12/2022	n/a		
R/0057	Renewal of the marketing authorisation.	13/10/2022	05/12/2022	SmPC, Annex II, Labelling and PL	Based on the review of data on quality, safety and efficacy, the CHMP considered that the benefit-risk balance of Shingrix in the approved indication remains favourable and therefore recommended the renewal of the marketing authorisation with unlimited validity.
IG/1575/G	This was an application for a group of variations. B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process	01/12/2022	n/a		

	of the AS				
WS/2325	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. B.II.b.5.z - Change to in-process tests or limits applied during the manufacture of the finished product - Other variation	17/11/2022	n/a		
II/0059/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.3.c - Change in the manufacturing process of the finished or intermediate product - The product is a biological/immunological medicinal product and the change requires an assessment of comparability	20/10/2022	n/a		
II/0054	Update of section 4.5 of the SmPC based on final results from study ZOSTER-059; this is a Phase IIIB, open label, randomised, controlled study to evaluate the immunogenicity, safety and reactogenicity of Shingrix when co-administered with Prevenar 13 in adults ≥ 50 years of age. In addition, the MAH took the opportunity to update section 4.5 of the SmPC to update the existing	20/10/2022	09/10/2023	SmPC	Section 4.5 of the SmPC has been updated to instruct prescribers that Shingrix can be given concomitantly with 13-valent pneumococcal conjugate vaccine (PCV13). For more information, please refer to the Summary of Product Characteristics.

	statement to specify the incidence percentages of fever and shivering upon co-administration of Shingrix with PPV23 based on study ZOSTER-035. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				
IB/0058/G	This was an application for a group of variations. B.II.b.3.a - Change in the manufacturing process of the finished or intermediate product - Minor change in the manufacturing process B.II.f.1.z - Stability of FP - Change in the shelf-life or storage conditions of the finished product - Other variation	15/07/2022	n/a		
IB/0056	B.II.b.3.z - Change in the manufacturing process of the finished or intermediate product - Other variation	22/06/2022	n/a		
IB/0055	C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation	19/05/2022	n/a		
II/0053	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	12/05/2022	n/a		
PSUSA/10678 /202110	Periodic Safety Update EU Single assessment - herpes zoster vaccine (recombinant, adjuvanted)	05/05/2022	n/a		PRAC Recommendation - maintenance

II/0052/G	This was an application for a group of variations. 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 B.II.b.1.c - Replacement or addition of a manufacturing site for the FP - Site where any manufacturing operation(s) take place, except batch release/control, and secondary packaging, for biol/immunol medicinal products or pharmaceutical forms manufactured by complex manufacturing processes	22/04/2022	n/a		
IB/0051	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	16/02/2022	n/a		
IB/0049	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		
PSUSA/10678 /202104	Periodic Safety Update EU Single assessment - herpes zoster vaccine (recombinant, adjuvanted)	28/10/2021	n/a		PRAC Recommendation - maintenance

II/0045	Update of section 4.4 of the SmPC in order to add a new warning on an increased risk of Guillain-Barré Syndrome (GBS) after vaccination with Shingrix observed in a post-marketing observational study in individuals aged 65 years or older. The RMP version 5.1 has also been approved. In addition, the MAH took the opportunity to make some editorial changes to the SmPC and to update the list of local representatives in the Package Leaflet. The PL has been updated accordingly 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	02/09/2021	04/04/2022	SmPC and PL	
IB/0047	B.II.b.4.f - Change in the batch size (including batch size ranges) of the finished product - The scale for a biological/immunological medicinal product is increased/decreased without process change (e.g. duplication of line)	29/06/2021	n/a		
IB/0046	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	02/06/2021	n/a		
PSUSA/10678 /202010	Periodic Safety Update EU Single assessment - herpes zoster vaccine (recombinant, adjuvanted)	06/05/2021	n/a		PRAC Recommendation - maintenance

IG/1379	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	30/03/2021	n/a		
WS/1961	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. B.II.b.3.a - Change in the manufacturing process of the finished or intermediate product - Minor change in the manufacturing process	25/03/2021	n/a		
II/0037	To update section 4.4 of the SmPC following the final results from study ZOSTER-064, listed as a category 3 study in the RMP; this is an observational study to assess frailty and other prognostic factors for development of herpes zoster in adult subjects who participated in studies ZOSTER-006 and ZOSTER-022 and the HZ efficacy, immunogenicity and safety of Shingrix by frailty status, in order to fulfil the post-authorisation measure MEA/FSR 012. The updated RMP version 4.1 has also been submitted. The MAH takes the opportunity to implement some editorial changes in Sections 4.4 and 5.1. and correction of the abbreviation CHO cells from Chinese Hamster Ovarian cells to Chinese Hamster Ovary cells in the Annex A.	11/03/2021	04/04/2022	SmPC	SmPC new text Deletion in section 4.4 of the reference to limited data to support the use of Shingrix in frail individuals including those with multiple comorbidities. For more information, please refer to the Summary of Product Characteristics.

	C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				
WS/1987	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. B.II.e.z - Change in container closure system of the Finished Product - Other variation	11/02/2021	n/a		
IB/0043	B.II.d.2.d - Change in test procedure for the finished product - Other changes to a test procedure (including replacement or addition)	05/02/2021	n/a		
WS/1949/G	This was an application for a group of variations following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. A.7 - Administrative change - Deletion of manufacturing sites B.II.b.3.z - Change in the manufacturing process of the finished or intermediate product - Other variation B.II.c.z - Change in control of excipients in the Finished Product - Other variation B.II.c.z - Change in control of excipients in the Finished Product - Other variation 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	14/01/2021	n/a		

	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 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 B.II.c.2.a - Change in test procedure for an excipient - Minor changes to an approved test procedure B.II.c.2.a - Change in test procedure for an excipient - Minor changes to an approved test procedure B.II.c.2.a - Change in test procedure for an excipient - Minor changes to an approved test procedure B.II.c.2.a - Change in test procedure for an excipient - Minor changes to an approved test procedure B.II.c.2.a - Change in test procedure for an excipient - Minor changes to an approved test procedure B.II.c.2.a - Change in test procedure for an excipient - Minor changes to an approved test procedure B.II.c.2.d - Change in test procedure for an excipient - Other changes to a test procedure (including replacement or addition)				
II/0036	C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority	14/01/2021	n/a		
IB/0039	B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS	16/12/2020	n/a		

PSUSA/10678 /202004	Periodic Safety Update EU Single assessment - herpes zoster vaccine (recombinant, adjuvanted)	29/10/2020	n/a		PRAC Recommendation - maintenance
II/0022	Extension of Indication to include a new population for Shingrix: adults 18 years of age or older at increased risk of Herpes Zoster supported by the clinical studies ZOSTER-002 (MEA 001), ZOSTER-039 (MEA 002), ZOSTER-041 (MEA 003), ZOSTER-028 (MEA 004), ZOSTER-001 and ZOSTER-015. As a consequence, sections 4.1, 4.2, 4.4, 4.8 and 5.1 of the SmPC are updated in order to delete a warning and to add new safety and efficacy information. The Package Leaflet is updated in accordance. The RMP version 2.2 has also been approved. In addition, the list of excipients has been updated in section 6 of the SmPC. Furthermore, the MAH took this opportunity to implement some editorial changes in Annex II and IIIA. C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one	23/07/2020	25/08/2020	SmPC and PL	Please refer to Scientific Discussion 'Shingrix-H-C-004336-II-0022'
II/0031	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	09/07/2020	n/a		

N/0032	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	01/07/2020	25/08/2020	Labelling and PL	
II/0030	B.II.b.3.c - Change in the manufacturing process of the finished or intermediate product - The product is a biological/immunological medicinal product and the change requires an assessment of comparability	18/06/2020	n/a		
II/0028	C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority	18/06/2020	n/a		
IA/0034/G	This was an application for a group of variations. 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.II.b.5.b - Change to in-process tests or limits applied during the manufacture of the finished product - Addition of a new test(s) and limits	12/06/2020	n/a		
IG/1244	B.II.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test procedure	12/06/2020	n/a		
PSUSA/10678 /201910	Periodic Safety Update EU Single assessment - herpes zoster vaccine (recombinant, adjuvanted)	14/05/2020	n/a		PRAC Recommendation - maintenance
II/0027/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	23/04/2020	n/a		

	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.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				
II/0026	B.II.b.3.c - Change in the manufacturing process of the finished or intermediate product - The product is a biological/immunological medicinal product and the change requires an assessment of comparability	17/04/2020	n/a		
IB/0029	B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS	16/04/2020	n/a		
II/0021	C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority	02/04/2020	n/a		
IA/0024	B.I.a.4.a - Change to in-process tests or limits applied during the manufacture of the AS - Tightening of in-process limits	07/02/2020	n/a		
IB/0025	B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure	05/02/2020	n/a		

IA/0020	B.II.b.5.a - Change to in-process tests or limits applied during the manufacture of the finished product - Tightening of in-process limits	12/12/2019	n/a		
IB/0019	B.I.a.4.z - Change to in-process tests or limits applied during the manufacture of the AS - Other variation	19/11/2019	n/a		
PSUSA/10678 /201904	Periodic Safety Update EU Single assessment - herpes zoster vaccine (recombinant, adjuvanted)	31/10/2019	n/a		PRAC Recommendation - maintenance
II/0016	Update of section 4.5 of the SmPC in order to reflect information related to coadministration based on the final results from studies ZOSTER-035 and ZOSTER-042; these are immunogenicity and safety studies in which Shingrix was co-administered either with Merck's 23-valent pneumococcal polysaccharide vaccine (Pneumovax 23; ZOSTER-035) or with GSK's reduced-antigen-content diphtheria and tetanus toxoids and acellular pertussis (dTpa) vaccine (Boostrix; ZOSTER-042); the Package Leaflet is updated accordingly. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	24/10/2019	24/03/2020	SmPC and PL	
II/0017	Update of sections 4.2 and 5.1 of the SmPC based on final results from study ZOSTER-048 (REC005); this is an immunogenicity and safety study of Shingrix in subjects previously vaccinated with Zostavax; the	19/09/2019	24/03/2020	SmPC and PL	Based on the final results from study ZOSTER-048 (REC005), an immunogenicity and safety study of Shingrix in subjects previously vaccinated with Zostavax, the SmPC sections 4.2 and 5.1 have been

	Package Leaflet is updated accordingly. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				updated as follows: Section 4.2: Shingrix can be given with the same schedule in individuals previously vaccinated with live attenuated HZ vaccine (see section 5.1). Section 5.1: In a phase III, open-label, multicentre clinical study (Zoster-048), a 2 doses schedule of Shingrix 2 months apart was assessed in 215 adults ≥65 years of age with a previous history of vaccination with live attenuated HZ vaccine ≥5 years earlier compared to 215 matched subjects who had never received live attenuated HZ vaccine. The immune response to Shingrix was unaffected by prior vaccination with live attenuated HZ vaccine. The PL has been updated accordingly.
IAIN/0015	B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site	16/05/2019	n/a		
PSUSA/10678 /201810	Periodic Safety Update EU Single assessment - herpes zoster vaccine (recombinant, adjuvanted)	16/05/2019	n/a		PRAC Recommendation - maintenance
II/0012	Update of section 4.8 of the SmPC in order to add "hypersensitivity reactions including rash, urticaria and angioedema" as an adverse drug reaction with frequency "rare". This update is based on data from clinical trials, literature and post-marketing surveillance reports. The Package Leaflet is updated accordingly. In addition, minor editorial changes were implemented	26/04/2019	24/03/2020	SmPC and PL	Since placing the product on the market, the MAH has received a total of 151 spontaneous reports containing one or more events of hypersensitivity. Of these reports, 15 were classified as limited and possible immediate (n=6) or delayed (n=9) allergic-type reactions described as rash, urticaria or angioedema. The events were limited to skin and/or sub-mucosal tissue. No cases classified as anaphylaxis were reported.

	throughout the Product Information. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				The CHMP considered that the data suggest that administration of Shingrix might trigger events with a presumed underlying IgE-mediated mechanism as well as delayed-type reactions, such as rash, urticaria and/or angioedema.
WS/1556/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.c.1.z - Change in the specification parameters and/or limits of an excipient - Other variation B.II.c.2.d - Change in test procedure for an excipient - Other changes to a test procedure (including replacement or addition) B.II.c.2.z - Change in test procedure for an excipient - Other variation	11/04/2019	n/a		
II/0011	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		
PSUSA/10678 /201804	Periodic Safety Update EU Single assessment - herpes zoster vaccine (recombinant, adjuvanted)	31/10/2018	n/a		PRAC Recommendation - maintenance
WS/1450	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.	18/10/2018	n/a		

	B.II.z - Quality change - Finished product - Other variation				
WS/1434	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. B.II.c.4.a - Change in synthesis or recovery of a non-pharmacopoeial or novel excipient - Minor change	27/09/2018	n/a		
II/0007	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	13/09/2018	n/a		
IA/0009	B.II.d.1.a - Change in the specification parameters and/or limits of the finished product - Tightening of specification limits	17/08/2018	n/a		
IB/0005	B.I.e.5.b - Implementation of changes foreseen in an approved change management protocol - Requires further supportive data	10/07/2018	n/a		
II/0001	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	28/06/2018	n/a		

	biological AS				
IB/0004	B.I.e.5.b - Implementation of changes foreseen in an approved change management protocol - Requires further supportive data	25/06/2018	n/a		
IB/0003	B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure	01/06/2018	n/a		
IB/0002	B.II.c.4.a - Change in synthesis or recovery of a non-pharmacopoeial or novel excipient - Minor change	30/04/2018	n/a		