EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Optaflu

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
T/0091	Transfer of Marketing Authorisation from Novartis Influenza Vaccines Marburg GmbH to Seqirus GmbH. Transfer of Marketing Authorisation	09/11/2016	12/12/2016	SmPC, Labelling and PL	
PSUSA/1745/ 201603	Periodic Safety Update EU Single assessment - influenza vaccine (surface antigen, inactivated, prepared in cell cultures)	29/09/2016	n/a		PRAC Recommendation - maintenance

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

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PSUSA/1745/201508	Periodic Safety Update EU Single assessment - influenza vaccine (surface antigen, inactivated, prepared in cell cultures)	17/03/2016	n/a		PRAC Recommendation - maintenance
PSUSA/1745/201504	Periodic Safety Update EU Single assessment - influenza vaccine (surface antigen, inactivated, prepared in cell cultures)	19/11/2015	22/01/2016	SmPC and PL	Refer to 'scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/1745/201504.
II/0086	B.I.a.5.a - Changes to the AS of a seasonal, prepandemic or pandemic vaccine against human influenza - Replacement of the strain(s) in a seasonal, prepandemic or a pandemic vaccine against human influenza	15/08/2015	25/08/2015	SmPC, Labelling and PL	
IB/0082	B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure	16/07/2015	n/a		
IB/0085	C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation	10/07/2015	n/a		
IB/0084	B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure	26/06/2015	n/a		
IAIN/0081/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 manufacture of a novel excipient	20/05/2015	25/08/2015	Annex II and PL	

	A.5.a - Administrative change - Change in the name and/or address of a manufacturer/importer responsible for batch release A.7 - Administrative change - Deletion of manufacturing sites				
T/0079	Transfer of Marketing Authorisation	08/04/2015	06/05/2015	SmPC, Labelling and PL	
IAIN/0080	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	26/03/2015	n/a		
PSUSA/1745/ 201408	Periodic Safety Update EU Single assessment - influenza vaccine (surface antigen, inactivated, prepared in cell cultures)	12/03/2015	n/a		PRAC Recommendation - maintenance
II/0077	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	26/01/2015	n/a		
II/0074/G	This was an application for a group of variations. 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	22/01/2015	n/a		

	biological AS B.I.d.1.c - Stability of AS - Change in the re-test period/storage period or storage conditions - Change to an approved stability protocol				
II/0071	Update of section 4.4 of the SmPC to add a warning on anxiety-related reactions. The Package Leaflet has been updated accordingly. In addition, the MAH took the opportunity to update the contact details for the local representative in Spain in the Package Leaflet. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	22/01/2015	06/05/2015	SmPC and PL	Syncope (fainting) can occur following, or even before, any vaccination as a psychogenic response to the needle injection. This can be accompanied by several neurological signs such as transient visual disturbance, paraesthesia and tonic-clonic limb movements during recovery. It is important that procedures are in place to avoid injury from faints.
PSUV/0070	Periodic Safety Update	20/11/2014	19/01/2015	SmPC and PL	Please refer to Optaflu PSUV-70 Scientific conclusions and grounds recommending the variation to the terms of the marketing authorisation.
IA/0078	B.II.f.1.e - Stability of FP - Change to an approved stability protocol	08/01/2015	n/a		
IB/0076	B.I.a.1.k - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - New storage site of MCB and/or WCB	23/12/2014	n/a		
II/0073	Substancial change to a test method for a biological active substance 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	18/12/2014	n/a		Substancial change to a test method for a biological active substance

	method or a method using a biological reagent for a biological AS				
IB/0072	B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS	04/11/2014	n/a		
II/0069	To update the product information to reflect that the strains are in accordance with the WHO recommendation and the EU decision for the 2014/2015 season. There is no change in the strains selected for the composition of the influenza vaccines compared to the previous season and the variation is therefore limited to an administrative update of the product information and a stability data update. In line with the adopted interim guidance on safety surveillance for seasonal influenza vaccines in the EU, an updated RMP including an enhanced safety surveillance plan is submitted. C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	24/07/2014	06/08/2014	SmPC, Labelling and PL	To update the product information to reflect that the strains are in accordance with the WHO recommendation and the EU decision for the 2014/2015 season. There is no change in the strains selected for the composition of the influenza vaccines compared to the previous season and the variation is therefore limited to an administrative update of the product information and a stability data update. In line with the adopted interim guidance on safety surveillance for seasonal influenza vaccines in the EU, an updated RMP including an enhanced safety surveillance plan is submitted.
IB/0068	B.I.a.4.z - Change to in-process tests or limits applied during the manufacture of the AS - Other variation	12/06/2014	n/a		
IB/0066/G	This was an application for a group of variations. B.I.d.1.c - Stability of AS - Change in the re-test period/storage period or storage conditions - Change to an approved stability protocol B.I.d.1.c - Stability of AS - Change in the re-test period/storage period or storage conditions - Change	07/05/2014	n/a		

	to an approved stability protocol				
II/0063	Update of sections 4.8 and 5.1 of the SmPC in order to update the efficacy and safety information based on the data from the phase III trial V8713 in adults, as requested by the CHMP in FUM039. 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	25/04/2014	06/08/2014	SmPC and PL	Study V58P13 is a large placebo controlled study. A total of 11376 subjects of the 11404 subjects enrolled were included in safety population. This study overall demonstrates vaccine efficacy compared to placebo, in a season where the predominant strain was H1N1 (VE = 83.8%; 97.5% CI lower limit: 61%). The safety findings are in line with the expected risk profile for any inactivated seasonal influenza vaccine and no new safety signals were detected. At the request of the CHMP the PI was updated with this information. The benefit/risk balance of the product remains positive.
II/0062	Changes in the manufacturing process of the active substance. B.I.a.2.c - Changes in the manufacturing process of the AS - The change refers to a [-] substance in the manufacture of a biological/immunological substance which may have a significant impact on the medicinal product and is not related to a protocol	25/04/2014	n/a		
IG/0426	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	11/04/2014	n/a		
PSUV/0057	Periodic Safety Update	06/03/2014	n/a		PRAC Recommendation - maintenance
II/0060	Update of sections 4.6 and 5.3 of the SmPC in order to include non-clinical data from a reproductive and developmental toxicity study. The Package Leaflet is updated accordingly. Furthermore, the PI is being	20/02/2014	06/08/2014	SmPC, Annex II, Labelling and PL	In a GLP-compliant reproductive and developmental toxicity study, the human dose of Optaflu was administered prior to and during gestation to female rabbits. Based on the data assessed, the CHMP concluded that i) no evidence of

	brought in line with the latest QRD template version 9. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				reproductive or developmental toxicity was seen in this study; ii) no effects on female fertility were observed whilst male fertility has not been assessed in animals; iii) there is no human data on use of Optaflu during lactation, however no effects on the breastfed newborn/infant are anticipated. Overall it was concluded that Optaflu is not a reproductive or developmental toxicant. The PI was updated accordingly.
IB/0061	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	31/01/2014	n/a		
IB/0059	B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS	10/01/2014	n/a		
IB/0058/G	This was an application for a group of variations. B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure	19/12/2013	n/a		
II/0056	Annual Strain Update B.I.a.5.a - Changes to the AS of a seasonal, prepandemic or pandemic vaccine against human influenza - Replacement of the strain(s) in a seasonal, prepandemic or a pandemic vaccine against human	07/10/2013	24/10/2013	SmPC, Labelling and PL	Update of the composition of the strains to those officially recommended by WHO and CHMP for the season 2013/2014, and these are the following: A/California/7/2009 (H1N1) pdm09-like strain A/Victoria/361/2011 (H3N2)-like strain

	influenza				B/Massachusetts/2/2012 (B strain)-like strain
IA/0054	A.4 - Administrative change - Change in the name and/or address of a manufacturer or supplier of the AS, starting material, reagent or intermediate used in the manufacture of the AS	03/07/2013	n/a		
IAIN/0055/G	This was an application for a group of variations. B.II.e.5.a.1 - Change in pack size of the finished product - Change in the number of units (e.g. tablets, ampoules, etc.) in a pack - Change within the range of the currently approved pack sizes B.II.e.5.a.1 - Change in pack size of the finished product - Change in the number of units (e.g. tablets, ampoules, etc.) in a pack - Change within the range of the currently approved pack sizes	20/06/2013	24/10/2013	SmPC, Labelling and PL	
IA/0053	A.4 - Administrative change - Change in the name and/or address of a manufacturer or supplier of the AS, starting material, reagent or intermediate used in the manufacture of the AS	22/05/2013	n/a		
II/0049	Update of section 4.8 of the SmPC in order to include angioedema in the summary of adverse reactions following a safety review. The Package Leaflet is updated accordingly. Editorial changes are included in sections 4.8 and 10 of the SmPC and the PL. C.I.4 - Variations related to significant modifications of the SPC due in particular to new quality, pre-clinical, clinical or pharmacovigilance data	25/04/2013	24/10/2013	SmPC and PL	A total of 42 spontaneous cases were reported through passive surveillance following the last influenza season. Of these 42 cases, 6 were suggestive of anaphylactic reaction based on signs and symptoms. Five cases were considered causally related to Optaflu. No increased frequency compared to expected post-vaccination background rates was observed. The adverse event 'angioedema' was consequently included in the table 'Summary of adverse reactions' in section 4.8 with the frequency 'not known (cannot be estimated from the available data)', and deleted

					from the Post marketing surveillance paragraph. The PL was updated accordingly
IB/0050	B.I.b.2.c - Change in test procedure for AS or starting material/reagent/intermediate - Other changes to a test procedure for a reagent, which does not have a significant effect on the overall quality of the AS	08/04/2013	n/a		
II/0047	B.I.a.2.c - Changes in the manufacturing process of the AS - The change refers to a [-] substance in the manufacture of a biological/immunological medicinal product and is not related to a protocol	21/02/2013	n/a		
IB/0045/G	This was an application for a group of variations. B.II.d.1.d - Change in the specification parameters and/or limits of the finished product - Deletion of a non-significant specification parameter (e.g. deletion of an obsolete parameter B.II.d.1.c - Change in the specification parameters and/or limits of the finished product - Addition of a new specification parameter to the specification with its corresponding test method B.II.d.1.c - Change in the specification parameters and/or limits of the finished product - Addition of a new specification parameter to the specification with its corresponding test method	08/02/2013	n/a		
IB/0042	B.II.z - Quality change - Finished product - Other variation	07/02/2013	n/a		
IAIN/0048/G	This was an application for a group of variations.	17/01/2013	n/a		

	C.I.9.a - Changes to an existing pharmacovigilance system as described in the DDPS - Change in the QPPV C.I.9.c - Changes to an existing pharmacovigilance system as described in the DDPS - Change of the back-up procedure of the QPPV C.I.9.d - Changes to an existing pharmacovigilance system as described in the DDPS - Change in the safety database C.I.9.g - Changes to an existing pharmacovigilance system as described in the DDPS - Change of the site undertaking pharmacovigilance activities C.I.9.h - Changes to an existing pharmacovigilance system as described in the DDPS - Other change(s) to the DDPS that does not impact on the operation of the pharmacovigilance system				
IAIN/0044/G	This was an application for a group of variations. C.I.9.g - Changes to an existing pharmacovigilance system as described in the DDPS - Change of the site undertaking pharmacovigilance activities C.I.9.h - Changes to an existing pharmacovigilance system as described in the DDPS - Other change(s) to the DDPS that does not impact on the operation of the pharmacovigilance system	11/10/2012	n/a		
IA/0041	B.II.e.6.b - Change in any part of the (primary) packaging material not in contact with the finished product formulation - Change that does not affect the product information	09/10/2012	n/a		
IB/0043	B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of	28/09/2012	n/a		

	the AS				
II/0040	Update of the composition of the strains for the season 2012/2013. B.I.a.5.a - Changes to the AS of a seasonal, prepandemic or pandemic vaccine against human influenza - Replacement of the strain(s) in a seasonal, prepandemic or a pandemic vaccine against human influenza	10/09/2012	20/09/2012	SmPC, Labelling and PL	Update of the composition of the strains to those officially recommended by WHO and CHMP for the season 2012/2013, and these are the following: A/California/7/2009 (H1N1)pdm09-like strain used (A/Brisbane/10/2010 wild type); A/Victoria/361/2011(H3N2)-like strain used (A/Victoria/361/2011, IVR-165); B/Wisconsin/1/2010-like strain used (B/Wisconsin/1/2010 wild type).
IA/0039	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	21/06/2012	n/a		
II/0034/G	This was an application for a group of variations. Change to quality control testing arrangements for the active substance. Change to a biological test procedure. B.I.b.2.d - Change in test procedure for AS or starting material/reagent/intermediate - Change (replacement) to a biological/immunological, immunochemical test method or a method using a biological reagent for a biological AS 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	21/06/2012	n/a		

	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				
IB/0038	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)	08/06/2012	n/a		
R/0033	Renewal of the marketing authorisation.	15/03/2012	25/05/2012	SmPC, Annex II, Labelling and PL	Taking into consideration all the available data gathered so far, the CHMP is of the opinion that there has been no change in the known benefits/risks and the uncertainties thereof since the granting of the marketing authorisation. Both the immunogenicity and safety profile of Optaflu, as described in the SmPC, has been confirmed by data from clinical trials and the experience in clinical practice submitted post approval, although limited. The CHMP therefore concluded that the benefit/risk assessment for Optaflu is favourable and has not changed since the original assessment therefore supporting the granting of a renewal of the marketing authorisation for use in the prevention of influenza in individuals 18 years of age and older. The CHMP recommended however that one additional five-year renewal on the basis of pharmacovigilance grounds is required. Considering the very limited post-marketing experience (only marketed on a very limited scale for one season), it is important that further safety information be collected following wider use of Optaflu in practice. Therefore, based upon the safety profile of Optaflu, the CHMP

					concluded that the MAH should continue to submit twice-yearly PSURs and should submit one additional renewal application in 5 years' time.
IA/0037	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	23/05/2012	n/a		
IB/0035/G	This was an application for a group of variations. 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 B.I.b.1.b - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Tightening of specification limits	11/04/2012	n/a		
IAIN/0036	B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site	15/03/2012	n/a		
II/0031	Update of the composition of the strains to those officially recommended by WHO and CHMP for the season 2010/2011. B.I.a.5.a - Changes to the AS of a seasonal, prepandemic or pandemic vaccine against human influenza - Replacement of the strain(s) in a seasonal,	03/11/2011	22/11/2011	SmPC, Labelling and PL	Update of the composition of the strains to those officially recommended by WHO and CHMP for the season 2010/2011. These are the following: A/California/7/2009 (H1N1)-like strain used A/Brisbane/10/2010 A/Perth/16/2009 (H3N2)-like strain used NYMC X-187

	prepandemic or a pandemic vaccine against human influenza				derived from A/Victoria/210/2009 B/Brisbane/60/2008
IA/0032	A.7 - Administrative change - Deletion of manufacturing sites	12/10/2011	n/a		
IA/0030/G	This was an application for a group of variations. C.I.9.a - Changes to an existing pharmacovigilance system as described in the DDPS - Change in the QPPV C.I.9.b - Changes to an existing pharmacovigilance system as described in the DDPS - Change in the contact details of the QPPV C.I.9.c - Changes to an existing pharmacovigilance system as described in the DDPS - Change of the back-up procedure of the QPPV C.I.9.e - Changes to an existing pharmacovigilance system as described in the DDPS - Changes in the major contractual arrangements with other persons or organisations involved in the fulfilment of pharmacovigilance obligations and described in the DD C.I.9.g - Changes to an existing pharmacovigilance system as described in the DDPS - Change of the site undertaking pharmacovigilance activities C.I.9.h - Changes to an existing pharmacovigilance system as described in the DDPS - Other change(s) to the DDPS that does not impact on the operation of the pharmacovigilance system	08/09/2011	n/a		
II/0028/G	This was an application for a group of variations. changes to the manufacturing process of the active	18/08/2011	n/a		

	substance B.I.a.2.c - Changes in the manufacturing process of the AS - The change refers to a [-] substance in the manufacture of a biological/immunological medicinal product and is not related to a protocol B.I.a.2.c - Changes in the manufacturing process of the AS - The change refers to a [-] substance in the manufacture of a biological/immunological medicinal product and is not related to a protocol				
IB/0029	B.II.b.1.b - Replacement or addition of a manufacturing site for the FP - Primary packaging site	18/08/2011	n/a		
IA/0027/G	This was an application for a group of variations. C.I.9.a - Changes to an existing pharmacovigilance system as described in the DDPS - Change in the QPPV C.I.9.c - Changes to an existing pharmacovigilance system as described in the DDPS - Change of the back-up procedure of the QPPV C.I.9.e - Changes to an existing pharmacovigilance system as described in the DDPS - Changes in the major contractual arrangements with other persons or organisations involved in the fulfilment of pharmacovigilance obligations and described in the DD C.I.9.f - Changes to an existing pharmacovigilance system as described in the DDPS - Deletion of topics covered by written procedure(s) describing pharmacovigilance activities C.I.9.g - Changes to an existing pharmacovigilance system as described in the DDPS - Change of the site	04/04/2011	n/a	Annex II	

	undertaking pharmacovigilance activities C.I.9.h - Changes to an existing pharmacovigilance system as described in the DDPS - Other change(s) to the DDPS that does not impact on the operation of the pharmacovigilance system				
IB/0026/G	This was an application for a group of variations. B.I.a.4.z - Change to in-process tests or limits applied during the manufacture of the AS - Other variation B.I.a.4.z - Change to in-process tests or limits applied during the manufacture of the AS - 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 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 B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure 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	04/03/2011	n/a		

IB/0025	B.I.a.3.e - Change in batch size (including batch size ranges) of AS or intermediate - The scale for a biological/immunological AS is increased/decreased without process change (e.g. duplication of line)	01/03/2011	n/a		
N/0023	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	27/01/2011	n/a		
IA/0024/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 supplier of the AS, starting material, reagent or intermediate used in the manufacture of the AS A.5.a - Administrative change - Change in the name and/or address of a manufacturer responsible for batch release	13/12/2010	n/a	Annex II and PL	
IA/0021	A.1 - Administrative change - Change in the name and/or address of the MAH	13/12/2010	n/a	SmPC, Labelling and PL	
IA/0022/G	This was an application for a group of variations. C.I.9.a - Changes to an existing pharmacovigilance system as described in the DDPS - Change in the QPPV C.I.9.c - Changes to an existing pharmacovigilance system as described in the DDPS - Change of the back-up procedure of the QPPV C.I.9.d - Changes to an existing pharmacovigilance system as described in the DDPS - Change in the safety database C.I.9.e - Changes to an existing pharmacovigilance	15/10/2010	n/a		

	system as described in the DDPS - Changes in the major contractual arrangements with other persons or organisations involved in the fulfilment of pharmacovigilance obligations and described in the DD C.I.9.f - Changes to an existing pharmacovigilance system as described in the DDPS - Deletion of topics covered by written procedure(s) describing pharmacovigilance activities C.I.9.g - Changes to an existing pharmacovigilance system as described in the DDPS - Change of the site undertaking pharmacovigilance activities C.I.9.h - Changes to an existing pharmacovigilance system as described in the DDPS - Other change(s) to the DDPS that does not impact on the operation of the pharmacovigilance system				
II/0017	Changes to the Homogeneity test evaluation of the monovalent bulk Change(s) to the test method(s) and/or specifications for the active substance	29/05/2009	16/06/2009		
II/0018	Change to the specification for the monovalent bulk Change(s) to the test method(s) and/or specifications for the active substance	23/04/2009	28/04/2009		
II/0016	Alternate down-stream process parameters for special strains Change(s) to the manufacturing process for the active substance	23/04/2009	28/04/2009		

N/0019	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	08/04/2009	n/a	PL	
IA/0020	IA_25_b_01_Change to comply with Ph. - compliance with EU Ph. update - active substance	25/03/2009	n/a		
IA/0015	IA_13_a_Change in test proc. for active substance - minor change	13/02/2009	n/a		
II/0012	Implementation of a new seed virus facility Quality changes	25/09/2008	02/10/2008		
IA/0014	IA_05_Change in the name and/or address of a manufacturer of the finished product	24/09/2008	n/a		
II/0011	Implementation of new type of syringe model with addition of 3 new presentations New presentation(s)	30/05/2008	10/07/2008	SmPC, Labelling and PL	
II/0008	Change(s) to the manufacturing process for the finished product	26/06/2008	03/07/2008		
IA/0013	IA_05_Change in the name and/or address of a manufacturer of the finished product	29/04/2008	n/a		
IB/0007	IB_38_b_Change in test procedure of finished product - minor change, biol. active subst./excipient	06/03/2008	n/a		
IA/0010	IA_09_Deletion of manufacturing site	05/03/2008	n/a		

IA/0009	IA_09_Deletion of manufacturing site	05/03/2008	n/a		
II/0003	Change(s) to the manufacturing process for the active substance	21/02/2008	26/02/2008		
IA/0006	IA_07_a_Replacement/add. of manufacturing site: Secondary packaging site	20/02/2008	n/a		
IA/0004	IA_05_Change in the name and/or address of a manufacturer of the finished product	14/02/2008	n/a		
SU/0002	Annual Strain Update. The Marketing Authorisation Holder (MAH) applied to update the composition of the strains of Optaflu to those officially recommended by WHO and CHMP for the season 2007/2008, and these are the following: - A/Solomon Islands/3/2006 (H1N1) like strain (A/Solomon Islands/3/2006, IVR-145) - A/Wisconsin/67/2005 (H3N2) like strain (A/Wisconsin/67/2005, NYMC X161B) - B/Malaysia/2506/2004 like strain (B/Malaysia/2506/2004). Annual Strain Update	13/12/2007	14/01/2008	SmPC, Labelling and PL	The MAH provided quality and clinical data in support of this variation. The clinical study in support of this variation aimed at evaluating the immunogenicity, tolerability and safety of the recommended vaccine virus composition for the 2007/2008 influenza season in two groups of healthy volunteers: adults aged ≥18 and ≤60 years and elderly aged >61 years. Overall, the submitted clinical documentation fulfils the criteria of the CPMP Note for Guidance on Harmonisation of Requirements for Influenza Vaccines (CPMP/BWP/214/96). However, the immune response to the B strain in elderly was considered marginal. Three weeks after vaccination the geometric mean titre (GMT) for the B strain in elderly was 40, i.e. the cut-off level generally used for seroprotection. In both age groups no severe or serious adverse reactions related to the vaccine occurred. Local and systemic tolerability also appeared acceptable, however a higher than expected rate of local pain at the injection site was observed, which is already included in the Product Information.