EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

IDflu

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
N/0048	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		PL	

[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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WS/1012	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. 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	10/11/2016	n/a		
PSUSA/1743/ 201603	Periodic Safety Update EU Single assessment - influenza vaccine (split virion, inactivated) (centrally authorised products only)	29/09/2016	n/a		PRAC Recommendation - maintenance
WS/0982	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.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	22/07/2016	09/08/2016	SmPC, Annex II, Labelling and PL	
PSUSA/1743/ 201508	Periodic Safety Update EU Single assessment - influenza vaccine (split virion, inactivated) (centrally authorised products only)	17/03/2016	n/a		PRAC Recommendation - maintenance
WS/0881/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	28/01/2016	n/a		

	B.I.b.z - Change in control of the AS - Other variation B.I.b.z - Change in control of the AS - Other variation B.I.b.z - Change in control of the AS - Other variation B.II.d.z - Change in control of the Finished Product - Other variation				
WS/0852	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	17/12/2015	n/a		
PSUSA/1743/ 201504	Periodic Safety Update EU Single assessment - influenza vaccine (split virion, inactivated) (centrally authorised products only)	06/11/2015	n/a		PRAC Recommendation - maintenance
WS/0763	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. Submission of a revised RMP version 10.0 in order to update: Part III/VI: - Strategy of the Enhanced Safety Surveillance in EEA during 2015-2016 influenza season presented;	24/09/2015	n/a		N/A

	- Status of GID47 updated and details on clinical study report provided in Appendix 9; - Results of THIN study removed from Appendix 9. Part V: - The table of risk minimization measures updated according to the PRAC assessment report of the RMP 8.0. 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				
WS/0814	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.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	13/08/2015	28/08/2015	SmPC, Labelling and PL	
IB/0039/G	This was an application for a group of variations. C.I.6.b - Change(s) to therapeutic indication(s) - Deletion of a therapeutic indication C.I.7.b - Deletion of a strength	12/06/2015	06/08/2015	SmPC, Labelling and PL	
WS/0701/G	This was an application for a group of variations following a worksharing procedure according to	23/04/2015	n/a		

	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.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				
PSUSA/1743/ 201408	Periodic Safety Update EU Single assessment - influenza vaccine (split virion, inactivated) (centrally authorised products only)	12/03/2015	n/a		PRAC Recommendation - maintenance
WS/0675/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. Group of variations to introduce 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 B.I.a.4.b - Change to in-process tests or limits	22/01/2015	n/a		

	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 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				
WS/0671	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. To implement a conformance process in order to be compliant with the industrial practises at drug product level. 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	22/01/2015	n/a		
IB/0035/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.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	15/01/2015	n/a		

	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.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.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure 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 to an approved stability protocol				
IB/0036/G	This was an application for a group of variations. A.7 - Administrative change - Deletion of manufacturing sites 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 B.II.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test procedure B.II.f.1.e - Stability of FP - Change to an approved stability protocol B.II.c.1.a - Change in the specification parameters and/or limits of an excipient - Tightening of	08/01/2015	n/a		

	specification limits B.II.d.1.a - Change in the specification parameters and/or limits of the finished product - Tightening of specification limits				
WS/0638	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. 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	18/12/2014	n/a		
PSUV/0027	Periodic Safety Update	04/12/2014	n/a		PRAC Recommendation - maintenance
IB/0030/G	This was an application for a group of variations. B.I.a.1.z - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Other variation 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.7 - Administrative change - Deletion of manufacturing sites	17/10/2014	n/a		
IAIN/0031	C.I.8.a - Introduction of or changes to a summary of Pharmacovigilance system - Changes in QPPV	15/10/2014	n/a		

	(including contact details) and/or changes in the PSMF location				
IB/0029	B.I.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation	07/10/2014	n/a		
II/0026	Changes to the product information in accordance with WHO recommendations. C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	24/07/2014	06/08/2014	SmPC, Labelling and PL	
PSUV/0024	Periodic Safety Update	10/04/2014	n/a		PRAC Recommendation - maintenance
IB/0025	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	17/01/2014	06/03/2014	SmPC, Labelling and PL	
R/0022	Renewal of the marketing authorisation.	25/07/2013	25/09/2013	Annex II	Annual influenza vaccination is the most effective method for preventing seasonal influenza virus and its complications. The benefit of IDflu/Intanza was established during clinical development and demonstrated the adequate immune response of both 9µg and 15µg formulations compared with the IM presentation. No new information regarding efficacy or effectiveness of IDflu/Intanza became available during the renewal period. The analysis of the safety information provided by the MAH in the clinical overview did not raise any new safety concern. The safety profile of IDflu/Intanza is well characterised and reflected in the PI. Among the unfavourable effects, severe allergic reactions are the only important identified risk included in the last version of the

					RMP. Encephalomyelitis, Guillain-Barre syndrome, Convulsion, Neuritis, Vasculitis and Thrombocytopenia are the important potential risks included in the last RMP. In addition, the MAH should submit a cumulative review of severe cutaneous reactions and infections and infestations in the next PSUR. Overall, the assessment of the benefit/risk balance for IDflu/Intanza remains positive.
II/0023	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 influenza	02/09/2013	09/09/2013	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-derived strain used (NYMC X-179A) A/Victoria/361/2011 (H3N2)-like strain used (NYMC X-223A) derived from A/Texas/50/2012 B/Massachusetts/02/2012
IB/0021	B.III.2.z - Change to comply with Ph. Eur. or with a national pharmacopoeia of a Member State - Other variation	27/02/2013	n/a		
II/0020	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	03/08/2012	22/08/2012	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-derived strain used (NYMC X-179A) A/Victoria/361/2011(H3N2)-derived strain used (IVR-165) B/Wisconsin/1/2010-like strain used (NYMC BX-39) derived from B/Hubei Wujiagang/158/2009
WS/0240	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.	19/04/2012	22/05/2012	SmPC and PL	The revised section 4.6 reflects that for Intanza/IDflu there is no clinical data on exposed pregnancies available. In line with the core SmPC, it also incorporates a paragraph

	Update of section 4.6 of the SmPC of Intanza 9 µg/IDflu 9µg to harmonise the recommendations for use of Intanza 9µg/IDFlu 9µg during pregnancy with the new European recommendations published by the CMD(h) for trivalent influenza vaccines in December 2011. In addition, the WSA took the opportunity to make minor linguistic corrections in the Portuguese translation. C.I.3.a - Implementation of change(s) requested following the assessment of an USR, class labelling, a PSUR, RMP, FUM/SO, data submitted under A 45/46, or amendments to reflect a Core SPC - Changes with NO new additional data are submitted by the MAH				detailing the available safety data gathered on trivalent inactivated influenza vaccines and reflects that inactivated influenza vaccines can be used in all stages of pregnancy. Larger datasets on safety are available for the second and third trimester, compared with the first trimester; however, data from worldwide use of inactivated influenza vaccines do not indicate any adverse foetal and maternal outcomes attributable to the vaccine. The PL was updated accordingly.
WS/0219	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. Update of sections 4.3, 4.4 and 4.8 of the SmPC in order to provide complementary information about the risk of allergic reactions and to reflect that there is very limited data in immunocompromised patients as requested by CHMP further to the assessment of PSUR 5. The package leaflet is updated accordingly. In addition, the WSA took the opportunity to update the list of local representatives in the Package Leaflet. Furthermore, the WSA proposed this opportunity to bring the PI in line with the latest QRD template version 8.1.	16/02/2012	19/03/2012	SmPC, Annex II, Labelling and PL	A cumulative review of cases of allergic reactions performed by the MAH covering the period from 24 February 2009 to 31 August 2011, and submitted within PSUR 6, identified 14 case reports of allergic reactions. Among them there were 2 anaphylactic reaction, 2 laryngeal oedema, 1 tongue oedema , 2 laryngeal oedema, and 1 lip swelling and 1 generalized urticaria. The information provided of the cases is considered scarce but a close temporal relationship with the vaccine administration was reported in all cases. Therefore, 'allergic reactions' have been included in the tabulated summary of adverse reactions in section 4.8 of the SmPC under 'Immune system disorders' with the frequency 'not known'. Section 4.3 and 4.4 are also revised to provide clearer and more detailed information about the risk of allergic reactions. Moreover, section 4.4 is updated to reflect there are very limited data available in immunocompromised

	C.I.3.b - Implementation of change(s) requested following the assessment of an USR, class labelling, a PSUR, RMP, FUM/SO, data submitted under Article 45/46, or amendments to reflect a Core SPC - Change(s) with new additional data submitted by the MAH				patients as requested by CHMP further to the assessment of PSUR 5. Safety data from PSUR 5 and PSUR 6, covering the period from 1st September 2010 to 30th April 2011 and from 1 May 2011 to 31 August 2011 respectively, did not raise any major safety concern and the safety profile of the vaccine has not been modified.
IA/0018	B.II.e.3.a - Change in test procedure for the immediate packaging of the finished product - Minor changes to an approved test procedure	14/02/2012	n/a		
WS/0204/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. Addition of a new building for the finished product manufacture. Increase in batch size for the finished product. B.II.b.3.c - Change in the manufacturing process of the finished product - The product is a biological/immunological medicinal product and the change requires an assessment of comparability B.II.b.4.c - Change in the batch size (including batch size ranges) of the finished product - The change requires assessment of the comparability of a biological/immunological medicinal product	19/01/2012	19/01/2012		
IB/0016	B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure	05/01/2012	n/a		

IA/0010	C.I.9.c - Changes to an existing pharmacovigilance system as described in the DDPS - Change of the back-up procedure of the QPPV	02/09/2011	n/a		
IB/0009	To update the product information to reflect that the strains are in accordance with the WHO recommendation and the EU decision for the 2011/2012 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. Changes to the contact details of the Bulgarian and Hungarian representatives in the package leaflet have also been included. C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	09/06/2011	n/a	SmPC, Labelling and PL	
IB/0008	B.II.d.2.d - Change in test procedure for the finished product - Other changes to a test procedure (including replacement or addition)	18/03/2011	n/a		
WS/0103/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. Change of identity test method used for the working seed lot and monovalent bulks.	17/03/2011	17/03/2011		

	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.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				
WS/0085	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. This was an application for a Type IB variation, following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	20/01/2011	28/02/2011	SmPC, Annex II and PL	The proposed group of variations WS-0085 was submitted for the implementation of the new QRD template version 7.3 and following the revision of the SmPC guideline. The version number of the detailed description of the pharmacovigilance system (DDPS) has also been removed from the Annex II.B as per recommendation from the EMA.
WS/0106	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. To add a quality control testing site for the finished product. B.II.b.2.a - Change to batch release arrangements and quality control testing of the FP - Replacement or addition of a site where batch control/testing	17/02/2011	17/02/2011		

	takes place				
WS/0067	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. A change in the manufacturing process of the Influenza Monovalent Bulks. 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	16/12/2010	16/12/2010		
IA/0007/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.i - Changes to an existing pharmacovigilance system as described in the DDPS - Change(s) to a DDPS following the assessment of the same DDPS in relation to another medicinal product of the same MAH C.I.9.c - Changes to an existing pharmacovigilance system as described in the DDPS - Change of the back-up procedure of the QPPV	11/11/2010	n/a	Annex II	
II/0006	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	06/08/2010	18/08/2010	SmPC, Labelling and PL	Update of the composition of the strains to those officially recommended by WHO and CHMP for the season 2010/2011, and these are the following: A/California/7/2009 (H1N1)-derived strain used NYMC X-179A

					A/Perth/16/2009 (H3N2)-like strain used NYMC X-187 derived from A/Victoria/210/2009 B/Brisbane/60/2008
II/0005	To implement a scale-up of the production of concentrated monovalent bulk. Change(s) to the manufacturing process for the active substance	18/03/2010	24/03/2010		
II/0004	To update section 5.1 and 4.8 of the SmPC for the 15 microgram strength in order to include data from a clinical study comparing aspects of efficacy and safety of the product with another influenza vaccine with a comparable indication in subjects over 64 years. In addition, the MAH used the opportunity of this variation to amend the Marketing Authorisation numbers and the Authorisation date in sections 8 and 9 of the SmPC and section 12 of the Labelling. The name of the European Medicines Agency has also been updated towards the product information. Update of Summary of Product Characteristics, Labelling and Package Leaflet	18/02/2010	23/03/2010	SmPC, Annex II, Labelling and PL	The dossier presented at the time of submission of the MAA included two confirmatory studies (GID16 and GID17) which showed the non-inferiority of the immunogenicity of the IDflu to a non-adjuvanted IM Influenza Vaccine (Vaxigrip) for each of the three strains in terms of post-vaccination GMTs. The MAH has provided the results of an additionnal study, FID01C, which compares the immunogenicity and the safety of the ID vaccine versus an adjuvanted (MF 59-containing) IM vaccine. Study FID01C was an open-label, multicentre, randomised, phase-3 study that compared IDflu 15 µg with an adjuvanted inactivated vaccine containing the same dosage of HA per strain. The data generated were in line with those described in the initial dossier submission, and showed that the ID vaccine was as immunogenic as the comparator vaccine. Both vaccines were generally well tolerated in this study. The safety profile of IDflu observed was in line with the one observed in the clinical trials described in the initial dossier application. The SmPC of IDflu 15 µg has been updated to add the immunogenicity data generated from study FID01C in section 5.1. In parallel, section 4.8 of the SmPC has been updated to reflect the comparison with an intramuscular adjuvanted vaccine.

					In addition, the Marketing Authorisation numbers and the Authorisation date in sections 8 and 9 of the SmPC and section 12 of the Labelling have been amended for both formulations. The name of the European Medicines Agency has also been updated towards the product information.
II/0003	To add new sources of Specified Pathogens Free (SPF) eggs used for influenza viral seed preparations. Update of or change(s) to the pharmaceutical documentation	18/02/2010	03/03/2010		
N/0001	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	08/04/2009	n/a	Labelling and PL	