Fluenz Tetra

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/0084	Update of section 4.6 of the SmPC to include new breast-feeding information based on a publication (Brady et al., 2018). The variation also includes recommendations from the renewal procedure (EMEA/H/C/002617/0079/R) to update sections 4.4 and 4.9 in relation to traceability and overdose, respectively, and to remove of the black triangle. In addition, the product information is updated based on the recommendations included in the Guideline on	17/01/2019		SmPC, Labelling and PL	Based on results from a randomised clinical trial comparing the safety and antibody responses to trivalent live attenuated intranasal vaccine versus inactivated influenza vaccine when administered to breastfeeding women (Brady et al., 2018), no firm conclusion can be made of transmission of vaccine virus from the vaccinated mother to the infant. Limited available evidence suggests that the trivalent Fluenz is not excreted in breastmilk.

[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).

30 Churchill Place ● Canary Wharf ● London E14 5EU ● United Kingdom
Telephone +44 (0)20 3660 6000 **Facsimile** +44 (0)20 3660 5520
Send a question via our website www.ema.europa.eu/contact

	quality aspects included in the product information for vaccines for human use (EMA/CHMP/BWP/133540/2017). The Package Leaflet is updated accordingly. In addition, the Marketing Authorisation Holder (MAH) took the opportunity to introduce minor editorial changes to the Product Information. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				
WS/1499	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. B.II.g.2 - Introduction of a post approval change management protocol related to the finished product	22/11/2018	n/a		
R/0079	Renewal of the marketing authorisation.	20/09/2018	20/11/2018		
II/0082	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	03/08/2018	28/08/2018	SmPC, Labelling and PL	
IG/0954	A.7 - Administrative change - Deletion of manufacturing sites	13/07/2018	n/a		

WS/1395	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.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS	28/06/2018	n/a		
II/0078/G	This was an application for a group of variations. B.I.a.2.b - Changes in the manufacturing process of the AS - Substantial change to the manufacturing process of the AS which may have a significant impact on the quality, safety or efficacy of the medicinal product 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.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.d - Change in the specification parameters and/or limits of an AS, starting	17/05/2018	n/a		

	material/intermediate/reagent - Deletion of a non-significant specification parameter (e.g. deletion of an obsolete parameter) B.I.b.1.d - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Deletion of a non-significant specification parameter (e.g. deletion of an obsolete parameter)				
IG/0907	B.II.d.1.a - Change in the specification parameters and/or limits of the finished product - Tightening of specification limits	26/03/2018	n/a		
II/0076	C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	22/03/2018	28/08/2018	SmPC and PL	There is a moderate amount of data from the use of Fluenz Tetra in pregnant women. There was no evidence of significant maternal adverse outcomes in 138 pregnant women who had a record of receiving trivalent Fluenz in a US based health insurance claims database. In more than 300 case reports in the MAH's safety database of vaccine administration to pregnant women, no unusual patterns of pregnancy complications or foetal outcomes were observed.
IB/0077	B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure	15/03/2018	n/a		
PSUSA/1742/ 201706	Periodic Safety Update EU Single assessment - influenza vaccine (intranasal, live attenuated)	11/01/2018	n/a		PRAC Recommendation - maintenance
II/0075/G	This was an application for a group of variations. B.I.a.2.a - Changes in the manufacturing process of	14/12/2017	n/a		

	the AS - Minor change in the manufacturing process of the AS B.I.a.2.b - Changes in the manufacturing process of the AS - Substantial change to the manufacturing process of the AS which may have a significant impact on the quality, safety or efficacy of the medicinal product				
IA/0073	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)	15/09/2017	n/a		
II/0072	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	28/07/2017	24/08/2017	SmPC, Labelling and PL	
PSUSA/1742/ 201612	Periodic Safety Update EU Single assessment - influenza vaccine (intranasal, live attenuated)	06/07/2017	n/a		PRAC Recommendation - maintenance
II/0064	C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority	05/05/2017	n/a		
IB/0071	B.II.c.2.d - Change in test procedure for an excipient - Other changes to a test procedure (including replacement or addition)	24/04/2017	n/a		
IB/0070	B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process	19/04/2017	n/a		

	of the AS				
IB/0069	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	19/04/2017	n/a		
IB/0068	B.II.d.2.d - Change in test procedure for the finished product - Other changes to a test procedure (including replacement or addition)	19/04/2017	n/a		
IA/0067/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) B.I.b.1.d - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Deletion of a non-significant specification parameter (e.g. deletion of an obsolete parameter)	31/03/2017	n/a		
T/0065	Transfer of Marketing Authorisation	28/02/2017	22/03/2017	SmPC, Labelling and	

				PL	
PSUSA/1742/ 201606	Periodic Safety Update EU Single assessment - influenza vaccine (intranasal, live attenuated)	12/01/2017	n/a		PRAC Recommendation - maintenance
IB/0063	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	06/01/2017	n/a		
IB/0062	B.II.d.2.d - Change in test procedure for the finished product - Other changes to a test procedure (including replacement or addition)	06/01/2017	n/a		
II/0061	Update of the RMP and of sections 4.3 and 4.8 of the SmPC to reflect that Fluenz Tetra is contraindicated only in children with severe hypersensitivity to eggs (instead of all children with egg allergy), and to update the safety information (update of the number of children and adolescents in the safety database). The PIL is amended accordingly. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	15/12/2016	22/03/2017	SmPC and PL	
IA/0060/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	07/10/2016	n/a		

	intermediate used in the manufacture of the AS or manufacturer of a novel excipient 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				
IAIN/0059	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	07/10/2016	22/03/2017	SmPC	
II/0057	Submission of a final study report for a post-authorisation safety study. C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority	15/09/2016	n/a		
II/0055	Submission of the final Clinical Study report for the PASS study number MA-VA-MEDI3250-1115: "A postmarketing Cohort Study of the Safety of Q/LAIV in Subjects 2 Through 49 Years of Age". C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority	15/09/2016	n/a		
II/0056	To update the annual strain for Fluenz Tetra for the season 2016-2017. B.I.a.5.a - Changes to the AS of a seasonal, prepandemic or pandemic vaccine against human	08/07/2016	29/07/2016	SmPC, Labelling and PL	

	influenza - Replacement of the strain(s) in a seasonal, prepandemic or a pandemic vaccine against human influenza				
PSUSA/1742/ 201512	Periodic Safety Update EU Single assessment - influenza vaccine (intranasal, live attenuated)	07/07/2016	n/a		PRAC Recommendation - maintenance
IB/0052/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	26/05/2016	n/a		
IA/0054	B.II.c.3.z - Change in source of an excipient or reagent with TSE risk - Other variation	10/05/2016	n/a		
IA/0053	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)	04/05/2016	n/a		
IB/0051	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	21/04/2016	n/a		
IB/0048	C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing	21/03/2016	n/a		

	authorisation, including the RMP - Other variation				
IB/0049	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	16/01/2016	29/07/2016	SmPC	
IB/0045	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	14/01/2016	29/07/2016	SmPC, Labelling and PL	
PSUSA/1742/ 201506	Periodic Safety Update EU Single assessment - influenza vaccine (intranasal, live attenuated)	14/01/2016	n/a		PRAC Recommendation - maintenance
IB/0047	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	18/12/2015	n/a		
II/0044	B.I.a.1.j - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Replacement or addition of a site where batch control/testing takes place and any of the test method at the site is a biol/immunol method	17/12/2015	n/a		
IG/0633	C.I.8.a - Introduction of or changes to a summary of Pharmacovigilance system - Changes in QPPV (including contact details) and/or changes in the PSMF location	09/12/2015	n/a		
IAIN/0043	B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site	16/10/2015	n/a		

II/0039	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	31/07/2015	28/08/2015	SmPC, Labelling and PL	
IB/0041	C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation	24/08/2015	n/a		
IB/0040	B.II.b.3.z - Change in the manufacturing process of the finished or intermediate product - Other variation	14/08/2015	n/a		
PSUSA/1742/ 201412	Periodic Safety Update EU Single assessment - influenza vaccine (intranasal, live attenuated)	09/07/2015	n/a		PRAC Recommendation - maintenance
IB/0037	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	08/07/2015	n/a		
IB/0038	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	02/06/2015	n/a		
IB/0036	B.I.a.2.z - Changes in the manufacturing process of the AS - Other variation	29/05/2015	n/a		

IB/0035/G	This was an application for a group of variations. B.I.a.4.a - Change to in-process tests or limits applied during the manufacture of the AS - Tightening of in-process limits B.I.a.4.b - Change to in-process tests or limits applied during the manufacture of the AS - Addition of a new in-process test and limits B.I.a.4.z - Change to in-process tests or limits applied during the manufacture of the AS - Other variation	29/05/2015	n/a		
II/0032/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 biological AS B.II.d.2.c - Change in test procedure for the finished product - Substantial change to or replacement of a biol/immunol/immunochemical test method or a method using a biol. reagent or replacement of a biol. reference preparation not covered by an approved protocol	21/05/2015	n/a		
IA/0033/G	This was an application for a group of variations. A.7 - Administrative change - Deletion of manufacturing sites A.7 - Administrative change - Deletion of	05/03/2015	n/a		

	manufacturing sites				
II/0031	B.I.c.1.b - Change in immediate packaging of the AS - Qualitative and/or quantitative composition for sterile and non-frozen biological/immunological ASs	26/02/2015	n/a		
PSUV/0023	Periodic Safety Update	09/01/2015	n/a		PRAC Recommendation - maintenance
IB/0030	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	07/01/2015	n/a		
II/0025/G	This was an application for a group of variations. A.7 - Administrative change - Deletion of manufacturing sites 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	18/12/2014	n/a		
IAIN/0029/G	This was an application for a group of variations. B.II.e.6.a - Change in any part of the (primary) packaging material not in contact with the finished product formulation - Change that affects the product information B.II.e.6.a - Change in any part of the (primary) packaging material not in contact with the finished	08/12/2014	28/08/2015	SmPC, Labelling and PL	

	product formulation - Change that affects the product information				
IB/0028/G	This was an application for a group of variations. B.I.a.3.a - Change in batch size (including batch size ranges) of AS or intermediate - Up to 10-fold increase compared to the originally approved batch size B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure	19/11/2014	n/a		
IB/0027	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	03/10/2014	n/a		
IA/0026	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)	03/10/2014	n/a		
IB/0024	B.II.b.3.z - Change in the manufacturing process of the finished or intermediate product - Other variation	19/09/2014	n/a		
IA/0021	B.II.b.3.a - Change in the manufacturing process of the finished or intermediate product - Minor change in the manufacturing process	12/08/2014	n/a		

II/0020	Seasonal update of the composition of the strains to those officially recommended by WHO and CHMP for the season 2014/2015, and these are the following: - A/California/7/2009 (H1N1)pdm09-like strain - A/Texas/50/2012 (H3N2)-like strain - B/Massachusetts/2/2012-like strain - B/ Brisbane/60/2008-like strain 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. 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	24/07/2014	06/08/2014	SmPC, Labelling and PL	Seasonal update of the composition of the strains to those officially recommended by WHO and CHMP for the season 2014/2015, and these are the following: - A/California/7/2009 (H1N1)pdm09-like strain - A/Texas/50/2012 (H3N2)-like strain - B/Massachusetts/2/2012-like strain - B/ Brisbane/60/2008-like strain 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.
PSUV/0016	Periodic Safety Update	10/07/2014	n/a		PRAC Recommendation - maintenance
IB/0019	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	11/06/2014	n/a		
IB/0018/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	04/06/2014	n/a		

	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.a.4.z - Change to in-process tests or limits applied during the manufacture 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				
IB/0015	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	24/04/2014	n/a		
IB/0014	B.II.b.3.z - Change in the manufacturing process of the finished or intermediate product - Other variation	09/04/2014	n/a		
IAIN/0013	B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site	28/03/2014	n/a		
IB/0012	B.II.f.1.e - Stability of FP - Change to an approved stability protocol	21/03/2014	n/a		
II/0005	Replacement or addition of a site where batch control/testing takes place. B.I.a.1.j - Change in the manufacturer of AS or of a	20/03/2014	n/a		

	starting material/reagent/intermediate for AS - Replacement or addition of a site where batch control/testing takes place and any of the test method at the site is a biol/immunol method				
II/0002	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	20/03/2014	n/a		
II/0001/G	This was an application for a group of variations. Replacement or addition of sites where batch control/testing takes place. B.I.a.1.j - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Replacement or addition of a site where batch control/testing takes place and any of the test method at the site is a biol/immunol method B.I.a.1.j - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Replacement or addition of a site where batch control/testing takes place and any of the test method at the site is a biol/immunol method	20/03/2014	n/a		
IB/0010	B.I.b.2.e - Change in test procedure for AS or starting material/reagent/intermediate - Other	06/03/2014	n/a		

	changes to a test procedure (including replacement or addition) for the AS or a starting material/intermediate				
IG/0405	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	26/02/2014	n/a		
IB/0007	B.II.f.1.z - Stability of FP - Change in the shelf-life or storage conditions of the finished product - Other variation	21/02/2014	06/08/2014	SmPC and PL	
IB/0003	B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS	12/02/2014	n/a		
IB/0009	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	10/02/2014	n/a		
IB/0004	B.I.a.4.z - Change to in-process tests or limits applied during the manufacture of the AS - Other variation	10/02/2014	n/a		
IB/0008	B.II.e.5.a.2 - Change in pack size of the finished product - Change in the number of units (e.g. tablets, ampoules, etc.) in a pack - Change outside the range of the currently approved pack sizes	07/02/2014	06/08/2014	SmPC, Labelling and PL	

IB/0006	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	31/01/2014	n/a		