EMA/656051/2020

Prepandrix

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
PSUSA/2281/ 201905	Periodic Safety Update EU Single assessment - pandemic influenza vaccine (H5N1) (split virion, inactivated, adjuvanted), prepandemic influenza vaccine (H5N1) (split virion, inactivated, adjuvanted)	28/11/2019	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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IA/0084	B.I.a.4.a - Change to in-process tests or limits applied during the manufacture of the AS - Tightening of in-process limits	26/07/2019	n/a		
WS/1670	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. B.II.z - Quality change - Finished product - Other variation	25/07/2019	n/a		
IA/0083/G	This was an application for a group of variations. A.7 - Administrative change - Deletion of manufacturing sites B.II.c.2.b - Change in test procedure for an excipient - Deletion of a test procedure if an alternative test procedure is already authorised	24/07/2019	n/a		
IG/1110	A.7 - Administrative change - Deletion of manufacturing sites	12/07/2019	n/a		
IG/1096	A.7 - Administrative change - Deletion of manufacturing sites	29/05/2019	n/a		
IB/0079	B.II.b.3.a - Change in the manufacturing process of the finished or intermediate product - Minor change in the manufacturing process	27/03/2019	n/a		
IB/0078/G	This was an application for a group of variations. B.I.z - Quality change - Active substance - Other	29/11/2018	n/a		

	variation B.I.z - Quality change - Active substance - Other variation B.I.a.4.a - Change to in-process tests or limits applied during the manufacture of the AS - Tightening of in-process limits				
PSUSA/2281/201805	Periodic Safety Update EU Single assessment - pandemic influenza vaccine (H5N1) (split virion, inactivated, adjuvanted), prepandemic influenza vaccine (H5N1) (split virion, inactivated, adjuvanted)	29/11/2018	n/a		PRAC Recommendation - maintenance
IB/0077	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	20/09/2018	13/09/2019	SmPC, Annex II, Labelling and PL	
II/0075/G	This was an application for a group of variations. A.7 - Administrative change - Deletion of manufacturing sites 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.f.1.b.5 - Stability of FP - Extension of the shelf life of the finished product - Biological/immunological medicinal product in accordance with an approved stability protocol B.II.b.2.b - Change to importer, batch release	25/05/2018	n/a		

	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				
PSUSA/2281/ 201705	Periodic Safety Update EU Single assessment - pandemic influenza vaccine (H5N1) (split virion, inactivated, adjuvanted), prepandemic influenza vaccine (H5N1) (split virion, inactivated, adjuvanted)	30/11/2017	n/a		Based on the review of data on quality, safety and efficacy, the CHMP considered that the benefit-risk balance of Prepandrix in the approved indication remains favourable and therefore recommended the renewal of the marketing authorisation with unlimited validity.
R/0071	Renewal of the marketing authorisation.	12/10/2017	28/11/2017	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 Prepandrix in the approved indication remains favourable and therefore recommended the renewal of the marketing authorisation with unlimited validity.
IB/0074	B.II.f.1.b.5 - Stability of FP - Extension of the shelf life of the finished product - Biological/immunological medicinal product in accordance with an approved stability protocol	23/11/2017	n/a		
IA/0072	A.7 - Administrative change - Deletion of manufacturing sites	30/06/2017	n/a		
IB/0070/G	This was an application for a group of variations. B.I.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation B.I.b.z - Change in control of the AS - Other variation	08/03/2017	n/a		

	B.II.a.z - Change in description and composition of the Finished Product - Other variation B.II.a.z - Change in description and composition of the Finished Product - Other variation B.II.b.z - Change in manufacture of the Finished Product - Other variation B.II.b.2.z - Change to importer, batch release arrangements and quality control testing of the FP - Other variation B.II.c.z - Change in control of excipients in the Finished Product - Other variation B.II.d.z - Change in control of the Finished Product - Other variation B.II.d.1.z - Change in the specification parameters and/or limits of the finished product - Other variation B.I.a.2.z - Changes in the manufacturing process of the AS - Other variation				
PSUSA/2281/ 201605	Periodic Safety Update EU Single assessment - pandemic influenza vaccine (H5N1) (split virion, inactivated, adjuvanted), prepandemic influenza vaccine (H5N1) (split virion, inactivated, adjuvanted)	01/12/2016	n/a		PRAC Recommendation - maintenance
IG/0717	B.II.e.2.c - Change in the specification parameters and/or limits of the immediate packaging of the finished product - Deletion of a non-significant specification parameter (e.g. deletion of an obsolete parameter)	01/09/2016	n/a		
IA/0068/G	This was an application for a group of variations. A.7 - Administrative change - Deletion of	24/08/2016	n/a		

	manufacturing sites 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.II.b.3.z - Change in the manufacturing process of the finished or intermediate product - Other variation				
IG/0679	B.II.e.2.b - Change in the specification parameters and/or limits of the immediate packaging of the finished product - Addition of a new specification parameter to the specification with its corresponding test method	01/06/2016	n/a		
IB/0064/G	This was an application for a group of variations. B.I.d.1.a.4 - Stability of AS - Change in the re-test period/storage period - Extension or introduction of a re-test period/storage period supported by real time data B.I.d.1.b.1 - Stability of AS - Change in the storage conditions - Change to more restrictive storage conditions of the AS	30/05/2016	n/a		
IG/0680	B.II.e.2.b - Change in the specification parameters and/or limits of the immediate packaging of the finished product - Addition of a new specification parameter to the specification with its corresponding test method	27/05/2016	n/a		
IB/0062	B.II.f.1.b.5 - Stability of FP - Extension of the shelf life of the finished product - Biological/immunological medicinal product in accordance with an approved	06/01/2016	n/a		

	stability protocol				
N/0063	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	14/12/2015	28/11/2017	PL	
PSUSA/2281/ 201505	Periodic Safety Update EU Single assessment - pandemic influenza vaccine (H5N1) (split virion, inactivated, adjuvanted), prepandemic influenza vaccine (H5N1) (split virion, inactivated, adjuvanted)	03/12/2015	n/a		PRAC Recommendation - maintenance
IB/0061	B.II.d.2.d - Change in test procedure for the finished product - Other changes to a test procedure (including replacement or addition)	06/08/2015	n/a		
IB/0059/G	This was an application for a group of variations. B.I.a.2.z - Changes in the manufacturing process of the AS - Other variation B.I.a.2.z - Changes in the manufacturing process of the AS - Other variation B.III.1.b.3 - Submission of a new/updated or deletion of Ph. Eur. TSE Certificate of Suitability - Updated certificate from an already approved manufacturer	29/04/2015	n/a		
IB/0058/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.c.1.c - Change in the specification parameters and/or limits of an excipient - Deletion of a non-significant specification parameter (e.g. deletion of	14/01/2015	n/a		

	an obsolete parameter)				
PSUV/0056	Periodic Safety Update	04/12/2014	n/a		PRAC Recommendation - maintenance
IG/0498	B.II.e.3.c - Change in test procedure for the immediate packaging of the finished product - Deletion of a test procedure if an alternative test procedure is already authorised	21/11/2014	n/a		
IG/0467	B.II.e.2.c - Change in the specification parameters and/or limits of the immediate packaging of the finished product - Deletion of a non-significant specification parameter (e.g. deletion of an obsolete parameter)	20/08/2014	n/a		
IG/0466/G	This was an application for a group of variations. B.II.e.2.c - Change in the specification parameters and/or limits of the immediate packaging of the finished product - Deletion of a non-significant specification parameter (e.g. deletion of an obsolete parameter) B.II.e.2.c - Change in the specification parameters and/or limits of the immediate packaging of the finished product - Deletion of a non-significant specification parameter (e.g. deletion of an obsolete parameter)	20/08/2014	n/a		
II/0051	To update section 4.4 of the SmPC to include a statement regarding the observed increased risk of narcolepsy following vaccination with Pandemrix, the MAH's ASO3 adjuvanted H1N1 influenza vaccine,	26/06/2014	27/05/2015	SmPC, Annex II and PL	Epidemiological studies relating to another AS03-adjuvanted influenza vaccine (Pandemrix H1N1, also manufactured in the same facility as Prepandrix), in several European countries have indicated an increased risk of

	based on a review of epidemiologic or post-marketing surveillance data. Furthermore, the MAH took this opportunity to bring the PI 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				narcolepsy with or without cataplexy in vaccinated as compared with unvaccinated individuals. In children/adolescents (aged up to 20 years), these studies have indicated an additional 1.4 to 8 cases in 100,000 vaccinated subjects. Available epidemiological data in adults aged over 20 years have indicated approximately 1 additional case per 100,000 vaccinated subjects. These data suggest that the excess risk tends to decline with increasing age at vaccination. There is currently no evidence to indicate that Prepandrix may be associated with a risk of narcolepsy.
IG/0446	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	24/06/2014	n/a		
II/0052/G	This was an application for a group of variations. Update of sections 4.2 and 5.1 of the SmPC in order to extend up to 12 months the interval between the two doses based on data from study D-PAN-H5N1-012 in adults. In addition some corrections to figures included in section 5.1 of the SmPC were introduced. 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 C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	20/03/2014	22/05/2014	SmPC and PL	The data assessed in this group of variations comprise additional efficacy and safety data from adult subjects in Study 012 who received Adjupanrix (A/Vietnam) and were subsequently boosted with A/Vietnam or A/Indonesia at 6 or 12 months. The immune response achieved with boosting at 12 months was comparable to that achieved with boosting at 6 months. This applies to both single and double priming regimens, and cross-protection for heterologous strains. There was no evidence of a waning of the priming effect over the 12 month period. The safety data support the favourable benefit-risk relationship for the regimens studied. The amendments proposed for the SmPC and PL were agreed.

IB/0050/G	This was an application for a group of variations. B.II.f.1.b.5 - Stability of FP - Extension of the shelf life of the finished product - Biological/immunological medicinal product in accordance with an approved stability protocol B.II.f.1.b.5 - Stability of FP - Extension of the shelf life of the finished product - Biological/immunological medicinal product in accordance with an approved stability protocol B.II.d.1.a - Change in the specification parameters and/or limits of the finished product - Tightening of specification limits B.II.d.1.z - Change in the specification parameters and/or limits of the finished product - Other variation	06/03/2014	22/05/2014	SmPC and PL	
PSUV/0049	Periodic Safety Update	18/12/2013	28/02/2014	SmPC and PL	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUV/0049.
IG/0306	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	12/06/2013	n/a		
R/0046	Renewal of the marketing authorisation.	15/11/2012	14/01/2013	SmPC, Annex II, Labelling and PL	Based upon the data that have become available since the granting of the initial Marketing Authorisation, the CHMP considers that the benefit-risk balance of Prepandrix remains positive, but considers that its safety profile is to be closely monitored for the following reasons: Considering the theoretical possibility that the AS03 adjuvant or some other vaccine component common to the marketing authorisation holder's pandemic influenza vaccines may have a role in the development of narcolepsy,

					this event is considered a potential risk for Prepandrix until epidemiological and mechanistic study data allow a conclusion on whether this risk may be applied to all AS03-adjuvanted pandemic influenza vaccines. Therefore, based upon the safety profile of Prepandrix, the CHMP concluded that the MAH should submit one additional renewal application in 5 years time.
IB/0045/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 supplier of the AS, starting material, reagent or intermediate used in the manufacture of the AS	20/09/2012	n/a		
IB/0044	B.II.d.2.d - Change in test procedure for the finished product - Other changes to a test procedure (including replacement or addition)	24/08/2012	n/a		
IB/0042/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 supplier of the AS, starting material, reagent or intermediate used in the manufacture of the AS	17/04/2012	n/a		

IA/0043	A.5.b - Administrative change - Change in the name and/or address of a manufacturer of the finished product, including quality control sites (excluding manufacturer for batch release)	26/03/2012	n/a		
II/0032	Shelf-Life extension of active substance B.I.d.1.a.3 - Stability of AS - Change in the re-test period/storage period - Extension of storage period of a biological/immunological AS not in accordance with an approved stability protocol	19/01/2012	19/01/2012		
IB/0030/G	This was an application for a group of variations. B.II.f.1.z - Stability of FP - Change in the shelf-life or storage conditions of the finished product - Other variation B.II.f.1.b.5 - Stability of FP - Extension of the shelf life of the finished product - Extension of storage period of a biological/immunological medicinal product in accordance with an approved stability protocol B.II.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test procedure A.7 - Administrative change - Deletion of manufacturing sites	13/01/2012	n/a		
WS/0161/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.	17/11/2011	22/12/2011		The proposed changes to the Product Information, to reflect post marketing experience with Pandemrix in SmPC sections 4.6 and 4.8, and to align the Product Information with wording in the Pandemrix and Pumarix Product

	Type II: to update sections 4.6 and 4.8 of the SmPC, with data on experience gained with Pandemrix, as requested by the CHMP in the 4th PSUR assessment for the AS03-adjuvanted H5N1 vaccine Marketing Authorisations. The PL is updated accordingly. 1st Type IB: to align the SmPC, labelling and PL texts for Prepandrix and Pandemic duplicate H5N1 licences, with wording present in the Pandemrix and Pumarix PI's. 2nd Type IB: to align the PL text for Prepandrix and Pandemic duplicate H5N1 licences with wording present in the Arepanrix and Pumarix PLs following readability testing. C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation C.I.4 - Variations related to significant modifications of the SPC due in particular to new quality, pre-clinical, clinical or pharmacovigilance data C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation				Informations were considered acceptable. Wording for SmPC section 6.6 (Special precautions for disposal and other handling) in the paragraphs in points 1 and 7 of 'Instructions for mixing and administration of the vaccine were further revised to add more clarity.
WS/0153	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 group of variations following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. Update of section 4.4 of the SmPC to	17/11/2011	22/12/2011	SmPC and PL	Based on a review of literature and a search in the global safety database performed by the MAH, the CHMP recommended including a wording on psychogenic syncope to the product information of the MAH injectable vaccines. The literature review showed an incidence peak occurred around the age of 15 years, with females having more than twice the incidence of males. The syncope reports with secondary injuries were reported most frequently in

	include a warning on psychogenic syncope based on the available safety data. The PL was proposed to be updated in accordance. In addition, the company took the opportunity to update the list of local representatives in the PL of Pumarix, Ambirix, Pandemrix, Pandemic influenza vaccine (H5N1) (split virion, inactivated, adjuvanted) GlaxoSmithKline Biologicals, Prepandrix and Fendrix. C.I.4 - Variations related to significant modifications of the SPC due in particular to new quality, pre-clinical, clinical or pharmacovigilance data				children and adolescents. Given that psychogenic syncope is not a true side effect, it was not considered appropriate to include syncope as an undesirable effect in section 4.8 of the SmPC. However, as such events can result in injury, and may not have occurred in the absence of the vaccination, the CHMP recommended to add a reference to such events in section 4.4 'Warning and Precaution' of the SmPC and in the PL.
IB/0039	B.II.f.1.b.5 - Stability of FP - Extension of the shelf life of the finished product - Extension of storage period of a biological/immunological medicinal product in accordance with an approved stability protocol	16/12/2011	03/07/2012	SmPC and PL	
IG/0133	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	22/11/2011	n/a		
II/0029	Update of section 5.1 'Pharmacodynamic Properties' of the SmPC to include persistence/booster data from - Study H5N1-009/022/023 (conducted in children 3-9 years of age): Persistence Month 24 - Study H5N1-002/030/038 (conducted in adults 18-60 years of age): Persistence Month 36 & Booster given at Month 36	20/10/2011	22/11/2011	SmPC	Immunogenicity and safety data at month 24 and 36 (including booster) were considered to be in line with the cumulative experience of the AS03-adjuvanted vaccines. There are no new concerns in view of immunogenicity and the reflection of the longer-term data from these studies in the SmPC was considered appropriate. In view of safety, no new concerns have arisen from these data that would require an update of the Product

	- Study H5N1-010 (in adults over 60 years of age): Persistence Month 24 C.I.4 - Variations related to significant modifications of the SPC due in particular to new quality, pre-clinical, clinical or pharmacovigilance data				Information at this stage.
IA/0031/G	This was an application for a group of variations. 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) 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.b - Change in the specification parameters and/or limits of the finished product - Tightening of specification limits for medicinal products subject to Official Batch Release	25/10/2011	n/a		
IA/0028	B.II.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test procedure	05/08/2011	n/a		
IB/0027	B.II.b.3.z - Change in the manufacturing process of the finished product - Other variation	19/07/2011	n/a		
IG/0081	C.I.9.c - Changes to an existing pharmacovigilance system as described in the DDPS - Change of the	07/07/2011	n/a		

	back-up procedure of the QPPV				
IG/0062/G	This was an application for a group of variations. 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.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	27/04/2011	n/a		
II/0026	To reflect new data obtained from study D-Pan H5N1-009 in section 4.2, 4.4, 4.8 and 5.1 of the SmPC, as well as in the patient leaflet (sections 3 and 4). This clinical study is conducted in children aged 3 to 9 years, to evaluate the immunogenicity, reactogenicity and safety of three formulations of AS03 adjuvanted H5N1 vaccine, given following a two dose schedule on Days 0 and 21.The MAH is also taking the opportunity of this procedure to update Annex II in order to reflect current information on the Pharmacovigilance System. C.I.4 - Variations related to significant modifications of the SPC due in particular to new quality, pre-clinical, clinical or pharmacovigilance data	17/03/2011	20/04/2011	SmPC, Annex II and PL	Concerning immune response, the D42 HI immune response parameters (SCR, SPR, SCF) did not clearly distinguish any one of the three formulations (Half HA/Half AS03, Full HA/Half AS03, Full HA/Full AS03) tested. However, the administration of a higher HA dose and, especially, the full adult dose, demonstrated advantages in terms of several HI and NA immune parameters. In particular, use of the adult dose gave improved HI responses to the heterologous strain and higher NA GMTs. Concerning safety, the greatest differences between the H5N1 vaccine and control groups in this study were seen when the adult dose was administered. Despite the greater local and general reactogenicity with the adult dose uptake of the second dose was very high and only four subjects did not complete both doses in the entire study. In addition the data do not indicate that higher reactogenicity was associated with SAEs.

					Overall, a difference in the frequency of adverse reactions between half adult and adult doses was observed after each dose. However, the administration of a second half adult or an adult dose did not enhance the reactogenicity, except for rates of general symptoms which were higher after the second adult dose.
IG/0052/G	This was an application for a group of variations. B.II.e.2.a - Change in the specification parameters and/or limits of the immediate packaging of the finished product - Tightening of specification limits B.II.e.2.b - Change in the specification parameters and/or limits of the immediate packaging of the finished product - Addition of a new specification parameter to the specification with its corresponding test method B.II.e.2.c - Change in the specification parameters and/or limits of the immediate packaging of the finished product - Deletion of a non-significant specification parameter (e.g. deletion of an obsolete parameter)	18/03/2011	n/a		
IB/0025	B.II.f.1.b.5 - Stability of FP - Extension of the shelf life of the finished product - Extension of storage period of a biological/immunological medicinal product in accordance with an approved stability protocol	21/10/2010	n/a		
II/0023	To amend section 6.6 of the Summary of Product Characteristics and to update Annex IIIA (labelling) of Product Information.	22/07/2010	26/08/2010	SmPC, Labelling and PL	

	C.I.4 - Variations related to significant modifications of the SPC due in particular to new quality, pre-clinical, clinical or pharmacovigilance data				
II/0022	To introduce an additional manufacturing site for the production of the antigen finished product. B.II.b.3.e - Change in the manufacturing process of the finished product - Introduction or increase in the overage that is used for the AS	22/07/2010	03/08/2010		
II/0021	To introduce an additional manufacturing site for the production of the adjuvant finished product. 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, batch control, and secondary packaging, for biological/immunological medicinal products.	22/07/2010	03/08/2010		
II/0020	To introduce an additional manufacturing site for the production of the adjuvant finished product. 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, batch control, and secondary packaging, for biological/immunological medicinal products.	22/07/2010	03/08/2010		
II/0019	To introduce an additional manufacturing site for the production fo the adjuvant finished product.	22/07/2010	03/08/2010		

	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, batch control, and secondary packaging, for biological/immunological medicinal products.				
II/0018	To introduce an additional manufacturing site for the production fo the adjuvant finished product. 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, batch control, and secondary packaging, for biological/immunological medicinal products.	22/07/2010	03/08/2010		
IB/0024	B.II.f.1.b.5 - Stability of FP - Extension of the shelf life of the finished product - Extension of storage period of a biological/immunological medicinal product in accordance with an approved stability protocol	23/07/2010	n/a	SmPC	
IB/0017	B.I.d.1.a.4 - Stability of AS - Change in the re-test period/storage period - Extension or introduction of a re-test period/storage period supported by real time data	23/06/2010	n/a		
II/0013	Change(s) to shelf-life or storage conditions	24/09/2009	19/10/2009	SmPC	
II/0015	To introduce some changes for the storage of the antigen.	24/09/2009	05/10/2009		

	Change(s) to container				
II/0010	To introduce some changes in the manufacturing process for the adjuvant emulsion at the bulk stage. Change(s) to the manufacturing process for the finished product	24/09/2009	05/10/2009		
IB/0016	IB_42_a_01_Change in shelf-life of finished product - as packaged for sale	30/09/2009	n/a		
IB/0014	IB_13_b_Change in test proc. for active substance - other changes (replacement/addition)	11/09/2009	n/a		
II/0012	To introduce some changes in the manufacturing site for the production of the active substance. Update of or change(s) to the pharmaceutical documentation	04/09/2009	08/09/2009		
II/0011	To introduce the use of alternative shipping containers to the manufacturing process for the active substance. Change(s) to container	20/08/2009	08/09/2009		
X/0004	To change the composition of the virus strain used in manufacture of Prepandrix active substance from A/VietNam/1194/2004 (H5N1) NIBRG-14 to A/Indonesia/05/2005 (H5N1) PR8-IBCDC-RG2. Annex I_1.(c) Replacement of a biological AS with	29/05/2009	07/08/2009	SmPC, Annex II, Labelling and PL	

	one of a slightly different molecular structure				
II/0009	To update sections 4.2, 4.4 and 5.1 of the SPC to include the possibility of a booster dose after primary immunisation with two doses of the marketing authorisation holder's (MAH) prepandemic vaccine containing antigen from the same subtype, based on data from clinical trials. The PL was updated accordingly. Paediatrics to validate Update of Summary of Product Characteristics and Package Leaflet	29/05/2009	07/07/2009	SmPC and PL	Based on immunogenicity and safety data from clinical trials, the product information was updated to reflect that a single dose of Pandemrix might be given to subjects who have previously received one or two doses of the MAH's AS03 adjuvanted prepandemic influenza vaccines. It has to be noted that the data are specific to the administration of H5N1 vaccine of a clade following one or two doses of H5N1 of a different clade.
II/0006	To update section 5.1 of the SPC regarding the interval between 2 doses for the primary schedule vaccination based on data from a clinical trial. The PL was updated to reflect the results of user testing. Update of Summary of Product Characteristics and Package Leaflet	29/05/2009	07/07/2009	SmPC and PL	In a clinical trial, two doses of A/Vietnam AS03 adjuvanted vaccine were needed to meet and exceed all three CHMP criteria for responses to homologous virus. The results were observed when the two doses were given either 21 days apart or 6 months apart. A single dose of A/Vietnam AS03 adjuvanted vaccine followed by a dose of A/Vietnam or A/Indonesia AS03 adjuvanted vaccine at Month 6 elicited haemagglutinin inhibition responses to homologous and heterologous booster strains that met and exceeded the CHMP criteria at Month 6 + 7 days post-boost with further increments at Month 6 + 21 days. Therefore based on immunogenicity and safety data, the product information was updated to reflect that two doses of AS03-adjuvanted vaccine given 6 months apart give comparable immune responses after the second dose to two doses given 21 days apart. The PL was updated further to a test performed to increase

					its readability.
II/0005	To extend the therapeutic indication to include treatment in subjects aged 61 years and above based on clinical trial data. Annex II and the PL were updated accordingly. The marketing authorisation holder took the opportunity to introduce minor corrections in the SPC and labeling and to correct the contact details for Cyprus, Denmark, Latvia and Slovakia in the PL. Extension of Indication	29/05/2009	07/07/2009	SmPC and PL	Please refer to the Scientific Discussion: Prepandrix-H-C-822-II-05-AR
II/0008	To introduce a change in the manufacturing process of the H5N1 antigen drug substance. Change(s) to the manufacturing process for the active substance	25/06/2009	01/07/2009		
II/0001	Introduction of an additional filling, labelling and packaging site for the adjuvanting system. Change(s) to the manufacturing process for the finished product	20/11/2008	15/12/2008		
IB/0003	IB_42_a_01_Change in shelf-life of finished product - as packaged for sale	29/09/2008	n/a		
IA/0002	IA_04_Change in name and/or address of a manuf. of the active substance (no Ph. Eur. cert. avail.)	30/07/2008	n/a	Annex II	