M-M-RVAXPRO

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/1937/ 201805	Periodic Safety Update EU Single assessment - measles / mumps / rubella vaccines (live, attenuated)	31/01/2019	08/04/2019	SmPC and PL	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/1937/201805.
WS/1578	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	04/04/2019	n/a		

[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).

	and/or limits of an AS, starting material/intermediate/reagent - Addition of a new specification parameter to the specification with its corresponding test method				
WS/1512	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. B.II.e.z - Change in container closure system of the Finished Product - Other variation	17/01/2019	n/a		
IG/0977	B.II.c.3.z - Change in source of an excipient or reagent with TSE risk - Other variation	19/10/2018	n/a		
IG/0973	A.7 - Administrative change - Deletion of manufacturing sites	21/09/2018	n/a		
IB/0088/G	This was an application for a group of variations. 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 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.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS	27/03/2018	n/a		

N/0087	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	19/02/2018	08/04/2019	Labelling	
WS/1325	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	18/01/2018	n/a		
IG/0856/G	This was an application for a group of variations. B.II.b.2.a - Change to importer, batch release arrangements and quality control testing of the FP - Replacement/addition of a site where batch control/testing takes place B.II.f.1.e - Stability of FP - Change to an approved stability protocol	10/11/2017	n/a		
II/0080	Update of section 4.8 of the SmPC to correct the frequency of the adverse reaction 'Fever (38.5°C or higher)' to 'very common'. In addition, the MAH took the opportunity to make some other editorial changes in the product information and to make corrections in the Finnish, Hungarian, Italian, Norwegian, Slovakian and Swedish product information. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	18/05/2017	15/12/2017	SmPC	

N/0084	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	24/03/2017	15/12/2017	PL	
IG/0777	A.1 - Administrative change - Change in the name and/or address of the MAH	23/02/2017	15/12/2017	SmPC, Labelling and PL	
WS/1029	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.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure	19/01/2017	n/a		
IG/0758	A.1 - Administrative change - Change in the name and/or address of the MAH	11/01/2017	15/12/2017	SmPC, Labelling and PL	
N/0081	Update of the package leaflet with revised contact details of the local representatives. Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	21/12/2016	15/12/2017	PL	
WS/0989	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	08/12/2016	n/a		

IG/0741	B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure	25/11/2016	n/a		
IG/0696	B.II.b.2.a - Change to importer, batch release arrangements and quality control testing of the FP - Replacement/addition of a site where batch control/testing takes place	20/06/2016	n/a		
IG/0695	B.II.b.3.a - Change in the manufacturing process of the finished or intermediate product - Minor change in the manufacturing process	08/06/2016	n/a		
IG/0687	B.II.b.3.a - Change in the manufacturing process of the finished or intermediate product - Minor change in the manufacturing process	30/05/2016	n/a		
IB/0073	B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS	10/03/2016	n/a		
PSUSA/1937/ 201505	Periodic Safety Update EU Single assessment - measles / mumps / rubella vaccines (live, attenuated)	14/01/2016	n/a		PRAC Recommendation - maintenance
IG/0625	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	16/11/2015	n/a		
WS/0786	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.	17/09/2015	n/a		

	B.II.c.z - Change in control of excipients in the Finished Product - Other variation				
N/0069	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	27/05/2015	15/12/2017	PL	
IG/0511	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	08/12/2014	n/a		
WS/0492	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. Update of section 4.8 of the ProQuad and M-M-RVaxpro SmPC to clarify that in severely immunocompromised individuals inadvertently vaccinated with measles-containing vaccine, measles inclusion body encephalitis, pneumonitis, and fatal outcome as a direct consequence of disseminated measles vaccine virus infection have been reported; disseminated mumps and rubella vaccine virus infection has also been reported. Further, minor editorial changes have been implemented in the Package Leaflet and SmPC for ProQuad, the M-M-RVaxpro annexes have been aligned with the latest QRD template version 9.0 and minor editorial changes implemented in the labelling for M-M-RVaxpro.	20/11/2014	09/04/2015	SmPC, Annex II, Labelling and PL	A published article, which described a study of more than two million children, suggested that MMR vaccines were not associated with an increased risk of encephalopathy after vaccination per se. However, measles inclusion body encephalitis, pneumonitis and death as a direct consequence of disseminated measles vaccine virus infection have been reported post-marketing in severely immunocompromised individuals that were - in spite of the contraindication - vaccinated with measles-containing vaccines. As a consequence, the existing statement in the product information concerning encephalitis and encephalopathy was clarified.

	C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				
IG/0493	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	21/10/2014	n/a		
IG/0487	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)	10/10/2014	n/a		
IB/0065	To add Merck Sharp and Dohme Corp., Vaccine Manufacturing Facility, 5325 Old Oxford Road, Durham, North Carolina, U.S. 27712 as finished product QC testing site for characteristics, restoration, pH, moisture and sterility. B.II.b.2.a - Change to importer, batch release arrangements and quality control testing of the FP - Replacement/addition of a site where batch control/testing takes place	02/09/2014	n/a		
IG/0435	A.1 - Administrative change - Change in the name and/or address of the MAH	06/05/2014	09/04/2015	SmPC, Labelling and PL	
IG/0429	A.5.b - Administrative change - Change in the name	16/04/2014	n/a		

	and/or address of a manufacturer/importer of the finished product, including quality control sites (excluding manufacturer for batch release)				
IG/0434	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	09/04/2014	n/a		
IB/0058/G	This was an application for a group of variations. B.II.d.2.d - Change in test procedure for the finished product - Other changes to a test procedure (including replacement or addition) B.II.d.1.z - Change in the specification parameters and/or limits of the finished product - Other variation	29/01/2014	n/a		
II/0057/G	This was an application for a group of variations. additional manufacturing site for finished product and change in immediate packaging of 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/control, and secondary packaging, for biol/immunol medicinal products or pharmaceutical forms manufactured by complex manufacturing processes B.II.e.1.a.3 - Change in immediate packaging of the finished product - Qualitative and quantitative composition - Sterile medicinal products and	18/12/2013	n/a		

	biological/immunological medicinal products				
IB/0056	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)	17/10/2013	n/a		
IB/0055	B.II.c.1.b - Change in the specification parameters and/or limits of an excipient - Addition of a new specification parameter to the specification with its corresponding test method	12/09/2013	n/a		
WS/0404/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. Update of analytical methods in order to align with compendial procedures and guidances 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 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	25/07/2013	n/a		
N/0052	Inclusion of additional local representative of the marketing authorisation holder for the new member state Croatia.	01/07/2013	09/04/2015	PL	

	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)				
IG/0312	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	13/06/2013	n/a		
WS/0349	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. change in the test procedure of the active substance 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	25/04/2013	n/a		
A20/0045	Art 20 review: Pursuant to Article 20 of Regulation (EC) No 726/2004, the European Commission requested on 15 March 2012, the opinion of the CHMP further to the evaluation of the most recent published data and post marketing surveillance regarding the vaccination with measles, mumps, rubella and varicella vaccines in pregnant women and immunocompromised subjects. The CHMP was requested to assess the impact thereof on the risk-benefit balance of M-M-RVAXPRO in these specific populations and to give its opinion whether the marketing authorisation of this product should be maintained, varied, suspended or withdrawn.	13/12/2012	20/02/2013	SmPC, Annex II and PL	Please refer to the Assessment Report: M-M-RVAXPRO-H-604-A20-45-Assessment Report-Article 20

IG/0261/G	This was an application for a group of variations. B.III.1.b.3 - Submission of a new or updated Ph. Eur. TSE Certificate of suitability - Updated certificate from an already approved manufacturer B.III.1.b.3 - Submission of a new or updated Ph. Eur. TSE Certificate of suitability - Updated certificate from an already approved manufacturer	30/01/2013	n/a		
IB/0048	B.II.b.1.z - Replacement or addition of a manufacturing site for the FP - Other variation	12/07/2012	n/a		
IA/0047	A.7 - Administrative change - Deletion of manufacturing sites	11/06/2012	n/a		
II/0042	Change in the manufacturer of a raw material for AS 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	19/04/2012	19/04/2012		
N/0043	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	16/04/2012	20/02/2013	PL	
IG/0156	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	24/02/2012	n/a		

	pharmacovigilance system				
II/0034	Change in the manufacturer of a raw material for AS 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	15/12/2011	15/12/2011		
IA/0035	B.III.1.b.3 - Submission of a new or updated Ph. Eur. TSE Certificate of suitability - Updated certificate from an already approved manufacturer	21/11/2011	n/a		
II/0033	Change in test procedure for the active substance. 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	17/11/2011	17/11/2011		
II/0031/G	This was an application for a group of variations. To introduce a change in a manufacturer of a raw material. -To submit updated TSE certificates of suitability for reagents. 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	22/09/2011	22/09/2011		

	[-] used in the manufacture of a biological/immunological product B.III.1.b.3 - Submission of a new or updated Ph. Eur. TSE Certificate of suitability - Updated certificate from an already approved manufacturer				
IG/0085	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)	08/07/2011	n/a		
R/0027	Renewal of the marketing authorisation.	17/03/2011	05/05/2011	SmPC, Annex II, Labelling and PL	During the renewal period no major change to the manufacture of the M-M-RVAXPRO was implemented. Taking into account all the variations and Follow-Up Measures (FUMs) that have been approved by the CHMP and given that the MAH commits to submit the data requested in the ongoing follow-up measures (FUMs that have not been fulfilled yet), it can be concluded that the product M-M-RVAXPRO conforms to the current CHMP quality guidelines. No change in the immunogenicity profile or efficacy of M-M-RVAXPRO was observed in clinical trials conducted since initial marketing authorisation. With respect to safety data no new specific safety concern was raised in clinical trials. The safety results provided in the PSUR data did not indicate any new safety signal or new adverse events, which are not covered in section 4.8 of the SmPC. Based on the data available the benefit/risk balance of M-M-RVAXPRO remains positive. The proposed SmPC, PIL and labelling were endorsed by the CHMP. The CHMP is of the opinion that the renewal can be granted with unlimited validity.
IA/0030/G	This was an application for a group of variations.	03/05/2011	n/a		

	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.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				
IB/0029	B.II.b.3.z - Change in the manufacturing process of the finished product - Other variation	29/04/2011	n/a		
IG/0059/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.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	15/04/2011	n/a		
IB/0028/G	This was an application for a group of variations. 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 B.II.d.2.d - Change in test procedure for the finished	17/12/2010	n/a		

	product - Other changes to a test procedure (including replacement or addition)				
WS/0044	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 change in the immediate packaging of the finished product. B.II.e.1.b.2 - Change in immediate packaging of the finished product - Type of container - Sterile medicinal products and biological/immunological medicinal products	23/09/2010	25/10/2010	SmPC and PL	
WS/0019/G	This was an application for a group of variations following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. B.I.a.2.c. Changes in the manufacturing process of the active substance. The change refers to a biological/immunological substance or use of a different chemically derived substance in the manufacture of a biological/immunological medicinal product and is not related to a protocol. B.I.a.4.b. Change to in-process tests or limits applied during the manufacture of the active substance. Addition of a new on-process test and limits. B.I.a.2.c - Changes in the manufacturing process of the AS - The change refers to a [-] substance in the	23/09/2010	23/09/2010		

	manufacture of a biological/immunological medicinal product and is not related to a protocol 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				
II/0024	To extend the indication to include administration to healthy children from 9 months of age under special circumstances, in accordance with official recommendations or when an early protection is considered necessary (e.g., day-care, outbreak situations, or travel to a region with high prevalence of measles). The MAH took further the opportunity to update Annex II to reflect the current version of the Risk Management Plan and to implement the new QRD templates. C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one	22/07/2010	06/09/2010	SmPC, Annex II and PL	For further information please refer to the Scientific Discussion: M-M-RVAXPRO-H-604-II-24-AR
WS/0018	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.2.e) Change in the test procedure for active substance or starting material/reagent/intermediate used in the manufacturing process of the active substance. Other changes to a test procedure (including replacement or addition) of the active substance or a starting material/intermediate.	22/07/2010	22/07/2010		

	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				
IA/0025	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	05/05/2010	n/a		
IA/0023/G	This was an application for a group of variations. To change in the name of the Drug substance and drug product manufacturer. Following the merger between Merck & Co., Inc. and Schering-Plough Corporation, the name of the company has changed from Merck & Co., Inc. to Merck Sharp & Dohme Corp. 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.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)	26/03/2010	n/a	Annex II	
II/0022	Change(s) to the manufacturing process for the finished product	18/03/2010	23/03/2010		
II/0021	To update section 4.5 of the SmPC to include information on the concomitant use of M-M-RVAXPRO	21/01/2010	15/03/2010	SmPC and PL	The modification sought within this variation was to obtain approval for the concomitant administration of MM-RVAXPRO

	with Prevenar and/or hepatitis A vaccine based on 4 clinical studies (P019, P066, P067 and P057). Section 2 of the PL was updated accordingly. In addition, the MAH took the opportunity to modify section 6.6 of the SmPC to improve the reconstitution instructions. Section 6 of the PL was updated in agreement to it. Update of Summary of Product Characteristics and Package Leaflet				with Prevenar and/or hepatitis A vaccine. Based on studies conducted with ProQuad (measles, mumps, rubella, and varicella virus vaccine) and M-M-RII/ M-M-RVAXPRO (measles, mumps and rubella) the clinical data analysed (protocols P019, P066, P067 and P057) confirmed that M-M-RVAXPRO can be administered concomitantly with hepatitis A vaccine (VAQTA) and pneumococcal conjugate vaccine (Prevenar-Pneumococcal 7-valent conjugate vaccine) without impairing antibody responses to measles, mumps, rubella, hepatitis A, or the serotypes of S. pneumoniae included in pneumococcal conjugate vaccine. The data also demonstrated that the concomitant administration of M-M-RVAXPRO with hepatitis A vaccine and pneumococcal conjugate vaccine had an acceptable safety profile. The results were appropriated to support concomitant administration of M-M-RVAXPRO with hepatitis A vaccine and pneumococcal conjugate vaccine. The vaccine demonstrated a favorable benefit/risk profile, and the proposed prescribing information for M-M-RVAXPRO was supported by the data analysed. No safety concern was established by the concomitant use of ProQuad/MMRVAXPRO, VAQTA and Prevenar.
II/0020	Update of the detailed description of pharmacovigilance system (DDPS) including the change of the Qualified Person Responsible for Pharmacovigilance (QPPV). The version number of the DDPS in Annex II has been updated accordingly. In addition, the MAH made minor amendments to the list of representatives of Denmark, Latvia and Malta in the Package Leaflet (PL).	17/12/2009	19/01/2010	Annex II and PL	The DDPS has been updated to version 2.0 in order to reflect the change of the QPPV as well as to notify other changes to the DDPS performed since the last approved version. Consequently, Annex II has been updated using the standard text including the new version number of the agreed DDPS. The CHMP considers that the Pharmacovigilance System as described by the MAH fulfils the requirements.

	Update of Summary of Product Characteristics, Labelling and Package Leaflet				
II/0019	Change(s) to the manufacturing process for the active substance	17/12/2009	06/01/2010		
II/0018	Change in the shelf - life of the active substance. Change(s) to shelf-life or storage conditions	22/10/2009	30/10/2009		
IA/0017	IA_22_a_Submission of TSE Ph. Eur. certificate for exc. - Approved/new manufacturer	09/06/2009	n/a		
IA/0016	IA_25_b_01_Change to comply with Ph. - compliance with EU Ph. update - active substance	25/03/2009	n/a		
II/0015	The Marketing Authorisation Holder applied for the addition of laboratories where test on importation takes place. Change(s) to the manufacturing process for the finished product	22/01/2009	28/01/2009		
II/0014	Changes to the manufacturing process of the drug product. Change(s) to the manufacturing process for the finished product	20/11/2008	02/12/2008		
II/0013	Addition of an alternative site (to perform manufacturing and release testing) .	24/07/2008	01/08/2008		

	Change(s) to the test method(s) and/or specifications for the finished product				
II/0011	Update to add epididymitis and pneumonia in section 4.8 of the SPC. In addition the list of all adverse events in section 4.8 was updated to a single list including adverse events from clinical studies and post marketing surveilance. The list of local representatives of the PL was updated to add Bulgaria and Romania and amend the contact details for Czech Republic, Denmark and Austria. Update of Summary of Product Characteristics and Package Leaflet	24/04/2008	20/06/2008	SmPC and PL	As a result of a review of adverse experiences reported for M -M-RVAXPO the CHMP agreed to include the adverse events pneumonia and epididymitis in the EU Product Information. Epididymitis is a common complication of infection by wild mumps virus and it was considered biologically possible that a small number of patients may develop similar complications after vaccination. In reviewing the spontaneous reports, from market introduction up until 10 September 2007, with more than 550 million doses distributed worldwide, 13 cases of epididymitis were identified that could be temporally associated with the administration of the M-M-R vaccine. Pneumonia is a common complication of infection by wild measles virus. After vaccination with any live virus vaccine, it is biologically possible that very few patients may develop respiratory complications ranging from mild upper respiratory infections to pneumonia. Reviewing the spontaneous reports, there were 7 cases of pneumonia temporally associated with the administration of M-M-R II, the nationally authorised predecessor vaccine to M-M-RVAXPRO produced using human serum albumin. The CHMP therefore agreed to include these events in the Product Information.
II/0012	During a mass vaccination campaign in adolescents and adults in Canada 6 cases of suspected anaphylactic reactions were reported. All cases were observed in young adults 18-30 years of age who each had a history of allergies. The symptoms were similar,	19/03/2008	18/04/2008	SmPC	During a mass vaccination campaign in adolescents and adults in Canada 6 cases of suspected anaphylactic reactions have been reported. All cases were observed in young adults 18-30 years of age who each had a history of allergies. The symptoms were similar (tingling in the mouth and throat,

	e.g. tingling in the mouth and throat, hoarseness, swelling in the throat, difficulty breathing, and occurred within 30 minutes following vaccination. All patients recovered after receiving treatment. The SPC was updated to reflect that adults and adolescents with a history of allergies may potentially be at increased risk of anaphylaxis or anaphylactoid reactions. Close monitoring is therefore recommended following vaccination for the early signs of such reactions. Update of Summary of Product Characteristics				hoarseness, swelling in the throat, difficulty breathing, among other symptoms) and occurred within 30 minutes following vaccination. All patients recovered after receiving treatment. The SPC was updated to reflect that adults and adolescents with a history of allergies may potentially be at increased risk of anaphylaxis or anaphylactoid reactions. Close monitoring is therefore recommended following vaccination for the early signs of such reactions.
IA/0010	IA_07_a_Replacement/add. of manufacturing site: Secondary packaging site	22/01/2008	n/a		
II/0008	Quality changes	20/09/2007	25/09/2007		
II/0006	To amend the Summary of Product Characteristics (SPC) sections 4.2, 4.4, 4.8 and 5.1 to add a new route of administration of the vaccine further to the CHMP assessment of Follow-Up Measure 13. The Labelling and Package Leaflet (PL) were updated accordingly. The MAH took the opportunity to correct the wording of section 4.1 of the SPC and accordingly section 1 of the PL. Additionally, the contact details of the local representatives for The Netherlands and Norway in section 6 of the PL were updated. Update of Summary of Product Characteristics, Labelling and Package Leaflet	24/05/2007	25/06/2007	SmPC, Labelling and PL	The immunogenicity and safety of M-M-RVAXPRO and VARIVAX when administered concomitantly by intramuscular (IM) route or subcutaneous (SC) route at two separate injection sites was assessed in healthy subjects 12 to 18 months of age. The study found no difference in immunogenicity between the two routes of administration. The general safety was comparable, however the frequencies of injection site reactions (such as redness or rashes at the injection site) were higher when the SC route was used instead of the IM route. The Product Information was updated to reflect that both routes of administration can be used, however the preferred route should be IM, except in subjects with coagulation

					disorders. A further change related to SPC Section 4.1 clarifying the use of M-M-RVAXPRO in outbreaks or post-exposure in line with section 4.2 of the SPC.
IA/0007	IA_15_a_Submission of Ph. Eur. certificate for active substance - approved manufacturer	22/05/2007	n/a		
II/0005	To add pruritus and vasculitis as potential adverse effects in the section 4.8 of the SPC following the update of the Company Core Data Sheet of M-M-RVAXPRO. The MAH took also the opportunity to correct minor spelling errors and to update the list of local representatives. Update of Summary of Product Characteristics, Labelling and Package Leaflet	22/03/2007	23/04/2007	SmPC, Annex II, Labelling and PL	Following the MAH's review of a summary of safety data of M-M-RVAXPRO and its component vaccines covering the period from 01 January 2006 to 04 May 2006 the CHMP agreed to include "pruritus" under the System Organ Class (SOC) "Skin and subcutaneous tissue disorders" and "vasculitis" under the SOC "Vascular disorders" under the sub-heading "Potential undesirable effects" in section 4.8 of the SPC.
IB/0004	IB_38_b_Change in test procedure of finished product - minor change, biol. active subst./excipient	30/01/2007	n/a		
N/0003	The MAH completed the list of local representatives in the PL to include the two new EU Member States (Bulgaria and Romania) according to the latest EMEA/QRD template. Furthermore the MAH took this oportunity to include the MA numbers in the labelling, to update the phone numbers of the local representatives and to make one minor correction in the PL Minor change in labelling or package leaflet not	29/01/2007	n/a	Labelling and PL	

	connected with the SPC (Art. 61.3 Notification)				
II/0001	Update of or change(s) to the pharmaceutical documentation	16/11/2006	n/a		
II/0002	Change(s) to the manufacturing process for the active substance	21/09/2006	27/09/2006		