EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Prevenar

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/02452	Periodic Safety Update EU Single assessment - PNEUMOCOCCAL POLYSACCHARIDE CONJUGATE VACCINE (7-VALENT, ADSORBED)	23/04/2015	22/06/2015	SmPC, Annex II and PL	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/02452.
N/0167	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	06/05/2014	22/06/2015	PL	
IA/0166	A.7 - Administrative change - Deletion of manufacturing sites	06/12/2013	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).

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II/0163/G	This was an application for a group of variations. Changes in the manufacturing process of the active substance and in the storage conditions. B.I.a.2.c - Changes in the manufacturing process of the AS - The change refers to a [-] substance in the manufacture of a biological/immunological medicinal product and is not related to a protocol B.I.a.2.c - Changes in the manufacturing process of the AS - The change refers to a [-] substance in the manufacture of a biological/immunological medicinal product and is not related to a protocol B.I.a.2.c - Changes in the manufacturing process of the AS - The change refers to a [-] substance in the manufacture of a biological/immunological medicinal product and is not related to a protocol B.I.d.1.b.3 - Stability of AS - Change in the storage conditions - Change in storage conditions of the AS	27/06/2013	n/a		
IB/0164/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.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.a.4 - Stability of AS - Change in the re-test period/storage period - Extension or introduction of a	30/05/2013	n/a		

	re-test period/storage period supported by real time data 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.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.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.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.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.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.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.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.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.3 - Stability of AS - Change in the storage conditions - Change in storage conditions of the AS B.I.d.1.b.3 - Stability of AS - Change in the storage conditions - Change in storage conditions of the AS B.I.d.1.b.3 - Stability of AS - Change in the storage conditions - Change in storage conditions of the AS B.I.d.1.b.3 - Stability of AS - Change in the storage conditions - Change in storage conditions of the AS B.I.d.1.b.3 - Stability of AS - Change in the storage conditions - Change in storage conditions of the AS B.I.d.1.b.3 - Stability of AS - Change in the storage conditions - Change in storage conditions of the AS B.I.d.1.b.3 - Stability of AS - Change in the storage conditions - Change in storage conditions of the AS				
IAIN/0165/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 A.5.a - Administrative change - Change in the name and/or address of a manufacturer responsible for batch release B.II.b.5.b - Change to in-process tests or limits applied during the manufacture of the finished product - Addition of a new tests and limits B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an	14/05/2013	n/a		

	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				
IG/0235/G	This was an application for a group of variations. C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation C.I.9.b - Changes to an existing pharmacovigilance system as described in the DDPS - Change in the contact details of the QPPV	06/12/2012	n/a		C.I.z - To replace the Detailed Description of the Pharmacovigilance System (DDPS) with the Pharmacovigilance System Master File (PSMF).
II/0161	Update of section 5.1 of the SmPC to align with the approved pneumonia efficacy information presented in the corresponding section of the Prevenar 13 SmPC (EMEA/H/C/1104). Post hoc analysis of the pneumonia efficacy data from the Northern California Kaiser Permanente trial currently presented is being replaced with the per-protocol, prespecified analysis, as reflected in the Prevenar 13 SmPC (official sponsor analysis). The MAH took the opportunity to revise the local representative details for Cyprus that are listed in the Package Leaflet. C.I.4 - Variations related to significant modifications of the SPC due in particular to new quality, pre-clinical, clinical or pharmacovigilance data	15/11/2012		SmPC and PL	In order to allow a correct interpretation of the data regarding the efficacy of the vaccines against pneumonia, the Prevenar SmPC was updated to include the same information as that approved in the Prevenar 13 SmPC (i.e. 35% [95% CI: 4, 56]) efficacy for pneumonia from the results from the primary analysis for efficacy against clinical pneumonia with abnormal chest x-ray in the per-protocol population in a large-scale, randomized, double-blind clinical trial. The current presented post hoc analysis of the pneumonia efficacy data from the Northern California Kaiser Permanente trial were replaced with the per-protocol, prespecified analysis, as reflected in the Prevenar 13 SmPC.
T/0159	Transfer of Marketing Authorisation from Wyeth Lederle Vaccines S.A. to Pfizer Limited.	24/05/2012	15/06/2012	SmPC, Labelling and	

	Transfer of Marketing Authorisation			PL	
IAIN/0160/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	06/06/2012	n/a		
IA/0157	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)	08/06/2011	n/a		
WS/0117	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. C.I.8.b - Introduction of a new Pharmacovigilance system - which has been assessed by the relevant NCA/EMA for another product of the same MAH	14/04/2011	06/05/2011		
R/0155	Renewal of the marketing authorisation.	16/12/2010	02/02/2011	SmPC, Annex II, Labelling and PL	Based on the CHMP review of the available information and on the basis of a re-evaluation of the benefit risk balance, the CHMP is of the opinion that the quality, safety and efficacy of this medicinal product continues to be adequately and sufficiently demonstrated and therefore considered that the

					benefit risk profile of Prevenar continues to be favourable. The CHMP is also of the opinion that the renewal can be granted with unlimited validity.
IA/0156	A.1 - Administrative change - Change in the name and/or address of the MAH	10/12/2010	n/a	SmPC, Annex II, Labelling and PL	
IA/0154	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	12/04/2010	n/a	Annex II	
IA/0153	C.I.9.g - Changes to an existing pharmacovigilance system as described in the DDPS - Change of the site undertaking pharmacovigilance activities	12/04/2010	n/a	Annex II	
IA/0152	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	12/04/2010	n/a	Annex II	
IA/0151	C.I.9.c - Changes to an existing pharmacovigilance system as described in the DDPS - Change of the back-up procedure of the QPPV	12/04/2010	n/a	Annex II	
IA/0150	C.I.9.a - Changes to an existing pharmacovigilance system as described in the DDPS - Change in the QPPV	12/04/2010	n/a	Annex II	
N/0149	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	22/03/2010	n/a	PL	

II/0148	Change(s) to the manufacturing process for the active substance	24/09/2009	08/10/2009		
II/0143	Change(s) to the manufacturing process for the active substance	23/07/2009	29/07/2009		
II/0142	To update section 4.8 of the Summary of the Product Characteristics (SPC) to include the term "flushing" further to the agreement of a follow up measure. The PL was updated accordingly. The MAH took the opportunity to update the information on the latex-free components of the existing container/closure system (plunger stopper and protective-tip cap) in section 6.5 of the Prevenar pre-filled syringe SPC. The telephone number of the local representative of the MAH for the UK was also updated. Update of Summary of Product Characteristics and Package Leaflet	25/06/2009	27/07/2009	SmPC and PL	As a Follow-Up Measure (FUM) the MAH carried out a comprehensive review of adverse events described as flush reactions that occur within minutes after the Prevenar injection and which disappear within 10-15 minutes. These reactions are sometimes limited to the injected thigh, sometimes spreading to the other thigh or the whole legs and sometimes the whole body. Therefore the "Undesirable effects" section was updated to include "flushing". As no events of flushing were identified in the Prevenar clinical trials the frequency of on "rare" adverse event was based on the calculation presented by the MAH. The CHMP further agreed to the MAH's proposal to include information on the latex free components of the prefilled syringe to assist the health care professionals when Prevenar is to be used in high risk group patients or a patient with know latex allergy.
II/0140	Change of test method for the finished product. Change(s) to the test method(s) and/or specifications for the finished product	25/06/2009	16/07/2009		
IA/0147	IA_43_a_01_ Add./replacement/del. of measuring or administration device - addition or replacement	08/07/2009	n/a		
II/0138	Update of the Detailed Description of the Pharmacovigilance System (DDPS) in order to reflect	29/05/2009	03/07/2009	Annex II	Update of the Detailed Description of the Pharmacovigilance System (DDPS) in order to reflect the change of Qualified

	the change of Qualified Person for Pharmacovigilance (QPPV). In addition, the Marketing Authorisation Holder (MAH) took the opportunity to make administrative and editorial changes to the DDPS. Consequently, Annex II has been updated using standard text including the new version number of the DDPS. Changes to QPPV Update of DDPS (Pharmacovigilance)				Person for Pharmacovigilance (QPPV). In addition, the Marketing Authorisation Holder (MAH) took the opportunity to make administrative and editorial changes to the DDPS. Consequently, Annex II has been updated using standard text including the new version number of the DDPS.
II/0139	Update of or change(s) to the pharmaceutical documentation	29/05/2009	16/06/2009		Additional testing facility for Prevenar final product containers.
IA/0146	IA_12_a_Change in spec. of active subst./agent used in manuf. of active subst. - tightening of spec.	10/06/2009	n/a		
IA/0145	IA_12_a_Change in spec. of active subst./agent used in manuf. of active subst. - tightening of spec.	10/06/2009	n/a		
IA/0144	IA_12_a_Change in spec. of active subst./agent used in manuf. of active subst. - tightening of spec.	10/06/2009	n/a		
IB/0141	IB_12_b_02_Change in spec. of active subst./agent in manuf. of active subst. - test parameter	05/05/2009	n/a		
II/0135	Introduction of an alternate method for the saccharide concentration in the conjugates Change(s) to the test method(s) and/or specifications for the active substance	19/03/2009	26/03/2009		

II/0136	Updated nephelometry assay for the determination of saccharide content. Change(s) to the test method(s) and/or specifications for the active substance	19/03/2009	25/03/2009		
II/0134	Alternative supplier for reagents and replacement of TSE certificate. Update of or change(s) to the pharmaceutical documentation	19/02/2009	09/03/2009		
II/0133	Change in the method for the determination of the enzymatic activity for diphtheria toxin in CRM197 protein. Change(s) to the test method(s) and/or specifications for the active substance	19/02/2009	09/03/2009		
II/0130	Change in sterlity testing of polysaccharides. Change(s) to the test method(s) and/or specifications for the active substance	19/02/2009	09/03/2009		
II/0131	The change of analitical method of active substance. Change(s) to the test method(s) and/or specifications for the active substance	22/01/2009	27/01/2009		
II/0129	Addition of an alternative testing method for in-process control of the active substance. Change(s) to the manufacturing process for the active	22/01/2009	27/01/2009		

	substance				
II/0119	Update of Summary of Product Characteristics, Annex II, Labelling and Package Leaflet. Update of section 4.5 of the SPC with information on the concomitant administration of Prevenar and Meningitec based on data from a clinical trial. In addition, the previously agreed class wording on apnoea was reflected in the PL as requested by the CHMP in July 2008. The MAH also took the opportunity of this variation to make linguistic corrections to the SPC, Annex II, Labelling and PL, as relevant, in all EU translations. Update of Summary of Product Characteristics and Package Leaflet	20/11/2008	06/01/2009	SmPC, Annex II, Labelling and PL	Concomitant administration of Prevenar (three doses at 2, 3.5, 6 months and a booster dose at approximately 12 months) and Meningitec (meningococcal C conjugate vaccine, two doses at 2 and 6 months and a booster dose at approximately 12 months) was assessed in a clinical trial. There was no evidence of immune interference between the two vaccines after the primary series nor after the booster doses. Further to the SPC update regarding the potential risk of apnoea in very premature infants, the PL was updated to inform that in babies born very prematurely (at or before 28 weeks of gestation) longer gaps than normal between breaths may occur for 2-3 days after vaccination.
II/0128	The Marketing Authorisation Holder applied for a change in the manufacturing process of the polysaccharides. Change(s) to the manufacturing process for the active substance	18/12/2008	05/01/2009		
IB/0132	IB_42_a_01_Change in shelf-life of finished product - as packaged for sale	19/12/2008	n/a	SmPC	
II/0124	Addition of a new manufacturing facility Change(s) to the manufacturing process for the active substance	20/11/2008	28/11/2008		

II/0111	Quality changes	20/11/2008	28/11/2008		
II/0125	Replace of a drug product release testing method with an improved one. Change(s) to the test method(s) and/or specifications for the active substance	25/09/2008	02/10/2008		
II/0122	Introduction of a new spectrophotometer used to monitor fermentation Quality changes	25/09/2008	02/10/2008		
II/0121	Changes to the specifications for raw materials Change to the test procedure and/or specification of a raw material	25/09/2008	02/10/2008		
IA/0127	IA_20_a_Change in test procedure for an excipient - minor change to approved test procedure	12/08/2008	n/a		
IA/0126	IA_19_a_Change in specification of an excipient - tightening of specification limits	01/08/2008	n/a		
II/0112	Update of or change(s) to the pharmaceutical documentation	24/07/2008	31/07/2008		
II/0120	Change to a test method used for release for polysaccharide-CRM 197 conjugates Change(s) to the test method(s) and/or specifications for the active substance	26/06/2008	04/07/2008		

II/0115	Quality changes	26/06/2008	04/07/2008		
IB/0123	Addition of a new test method and specification for release of purified pneumococcal polysaccharides. IB_12_b_02_Change in spec. of active subst./agent in manuf. of active subst. - test parameter	02/07/2008	n/a		
II/0107	To update section 4.8 of the SPC to include the term "crying". The PL is updated accordingly. Update of Summary of Product Characteristics and Package Leaflet	24/04/2008	20/06/2008	SmPC and PL	A review of case reports indicated that a causal association existed between Prevenar administration and crying. The review identified reports of crying coincident with pneumococcal 7-valent conjugate vaccine administration. In the majority of reports, the patient received either concomitant vaccine and/or concomitant drug administration; however, in some of the reports of crying only administration of pneumococcal 7-valent conjugate vaccine was listed. The term ” crying” was included as a very common adverse event.
II/0118	Changes to the pre-filled syringe Change(s) to container	30/05/2008	11/06/2008		
II/0116	Introduction of an alternative filling process Change(s) to the manufacturing process for the finished product	30/05/2008	11/06/2008		
II/0114	Change(s) to the manufacturing process for the active substance	19/03/2008	28/03/2008		
IA/0117	IA_41_a_01_Change in pack size - change in no. of units within range of appr. pack size	17/03/2008	17/03/2008	SmPC, Labelling and	

				PL	
II/0102	Update of Summary of Product Characteristics and Package Leaflet To update sections 4.2 “Posology and method of administration”, 4.4 “Special warnings and precautions for use” and 5.1 “Pharmacodymanic properties” with immunogenicity and effectiveness data on the infant 3-dose primary vaccination schedule. The Package Leaflet is changed accordingly. Update of Summary of Product Characteristics and Package Leaflet	13/12/2007	06/02/2008	SmPC and PL	The CHMP has previously asked the MAH to submit this type II variation in order to reflect information on a “2+1” infant primary vaccination schedule (2x priming + 1 boost) in section 4.2 of the SPC, as new data has become available and several EU countries (Belgium, Denmark, Italy, Norway, and the United Kingdom) have already implemented such a schedule, or have the intention to implement it. The MAH has submitted data from randomised, controlled studies comparing the immunogenicity of “3+1” and “2+1” schedules; open studies comparing immunogenicity after the second and the third dose of a three-dose infants series as well as open, uncontrolled studies of the immunogenicity of the “2+1” schedule and further literature data. From the presented data it can be summarised that overall after a 2-dose schedule the antibody titre for 6B and 23F seems to be lower than with a 3-dose primary vaccination schedule. In addition in all trials this lower immunogenicity for 6B and 23F led to an equal boostability between both schedules and no evidence has led to the conclusion that the 2-dose primary vaccination schedule has a higher risk of breakthrough cases. The Product Information was updated to reflect this information.
II/0105	Change(s) to the manufacturing process for the active substance	24/01/2008	29/01/2008		
IA/0113	IA_23_b_Change in source of excip./reagent to veg./synthetic material - other cases	10/01/2008	n/a		

II/0108	Change(s) to the test method(s) and/or specifications for the active substance	13/12/2007	19/12/2007		
IB/0110	IB_12_b_02_Change in spec. of active subst./agent in manuf. of active subst. - test parameter	19/12/2007	n/a		
II/0109	Update of sections 4.4 "Special warnings and precautions for use" and 4.8 Undesirable effects" of the Summary of Product Characteristics to implement the class labelling text on the risk of apnoea following vaccination of very prematurely born infants agreed by the CHMP in July 2007. Update of Summary of Product Characteristics	15/11/2007	11/12/2007	SmPC	Following a review on the risk of apnoea in very premature infants after immunisation the CHMP recommended a class labelling on apnoea for all vaccines in very premature infants. The SPC was updated to include information about the potential risk of apnoea and the need for respiratory monitoring for 48-72h, when the primary immunisation series is administered to very premature infants (born ? 28 weeks of gestation) and particularly for those with a previous history of respiratory immaturity. Nonetheless, preterm infants should not be withdrawn from the immunisation scheme because the benefit of vaccination outweighs the risk of apnoea.
II/0103	Change(s) to the test method(s) and/or specifications for the finished product	18/10/2007	23/10/2007		
X/0091	Annex I_1.(c) Replacement of a biological AS with one of a slightly different molecular structure	21/06/2007	31/08/2007	Annex II	
IA/0104	IA_23_b_Change in source of excip./reagent to veg./synthetic material - other cases	31/08/2007	n/a		
IA/0101	IA_16_b_Submission of new TSE certificate relating to active substance - other substances	02/08/2007	n/a		
II/0100	Change(s) to the test method(s) and/or specifications	19/07/2007	01/08/2007		

	for the active substance				
II/0095	To amend section 5.3 of the SPC to include information from two repeated dose toxicity studies with Prevenar in rats and monkeys. Update of Summary of Product Characteristics	21/06/2007	30/07/2007	SmPC	The repeated dose toxicity studies with Prevenar in both rats and monkeys showed local inflammatory reactions with evidence of reversibility. No adverse systemic effects were observed. Local inflammatory reactions at the injection site have been reported in humans and are adequately reflected in section 4.8 of the SPC. The section 5.3 was updated to inform that no evidence of any significant local or systemic toxic effects were revealed in repeated dose subcutaneous toxicitiy studies in rats and monkeys.
IB/0099	IB_15_b_01_Submission of Ph. Eur. certificate for active substance - new manuf./sterile substance	06/06/2007	n/a		
IB/0097	IB_25_a_01_Change to comply with Ph. - compliance with EU Ph. - active substance	07/05/2007	n/a		
IA/0098	IA_31_a_Change to in-process tests/limits during manufacture - tightening of in-process limits	07/05/2007	n/a		
II/0094	Change(s) to the test method(s) and/or specifications for the finished product	26/04/2007	02/05/2007		
II/0093	Change(s) to the test method(s) and/or specifications for the finished product	26/04/2007	02/05/2007		
IA/0096	IA_38_a_Change in test procedure of finished product - minor change to approved test procedure	11/04/2007	n/a		
II/0080	To extend the therapeutic indication from active immunisation against bacteraemic pneumonia to	22/02/2007	02/04/2007	SmPC and PL	For further information please refer to the Scientific Discussion: EMEA-H-323-II-80-AR

	active immunisation against pneumonia. The Package Leaflet (PL) was updated in accordance with the changes proposed to the Summary of Product Characteristics. The MAH also took the opportunity to amend the PL to update the contact details of the local representative in Iceland. Extension of Indication				
II/0090	To change Sections 4.4 "Special warnings and precautions for use" and 5.1"Pharmacodynamic Properties" of the Summary of Product Characteristics to include information on Safety and Immunogenicity of Prevenar in Infants with Sickle Cell disease further to the CHMP assessment of a study on sickle cell disease in children. The Package Leaflet was updated accordingly. Update of Summary of Product Characteristics and Package Leaflet	24/01/2007	09/03/2007	SmPC and PL	Children with sickle cell disease (SCD) are at marked increased risk for invasive pneumococcal disease (about 22-fold higher than the general population). The results of a study submitted by the MAH have demonstrated that Prevenar administered at 2, 3, 4 months of age in infants with SCD was well tolerated, sufficiently immunogenic and induced immune memory. These study results were also supported by various publications on vaccination of infants and children with SCD.
II/0076	In addition, the MAH completed the the list of local representatives in the PL to include the two new member states (Bulgaria and Romania). Extension of Indication	24/01/2007	09/03/2007	SmPC and PL	For further information please refer to the Scientific Discussion: EMEA-H-323-II-76-AR
II/0092	Change(s) to the manufacturing process for the active substance	22/02/2007	27/02/2007		
II/0089	Change to the test procedure and/or specification of a raw material	22/02/2007	27/02/2007		

II/0087	Change(s) to the manufacturing process for the active substance	22/02/2007	27/02/2007		
II/0088	Change(s) to the manufacturing process for the finished product	16/11/2006	22/11/2006		
II/0075	Change(s) to the manufacturing process for the active substance	16/11/2006	22/11/2006		
IB/0086	IB_38_b_Change in test procedure of finished product - minor change, biol. active subst./excipient	22/11/2006	n/a		
II/0082	Update of or change(s) to the pharmaceutical documentation	18/10/2006	24/10/2006		
II/0078	Change(s) to the test method(s) and/or specifications for the finished product	21/09/2006	26/09/2006		
IA/0083	IA_31_a_Change to in-process tests/limits during manufacture - tightening of in-process limits	15/08/2006	n/a		
IA/0081	IA_31_a_Change to in-process tests/limits during manufacture - tightening of in-process limits	07/08/2006	n/a		
IA/0079	IA_16_b_Submission of new TSE certificate relating to active substance - other substances	19/07/2006	n/a		
IB/0074	IB_38_b_Change in test procedure of finished product - minor change, biol. active subst./excipient	16/06/2006	n/a		
IA/0077	IA_43_a_01_ Add./replacement/del. of measuring or administration device - addition or replacement	13/06/2006	n/a		

IB/0073	IB_38_b_Change in test procedure of finished product - minor change, biol. active subst./excipient	16/05/2006	n/a		
II/0072	Change(s) to the manufacturing process for the active substance	27/04/2006	02/05/2006		
II/0070	Change(s) to the manufacturing process for the active substance	27/04/2006	02/05/2006		
II/0068	Change(s) to the test method(s) and/or specifications for the active substance	27/04/2006	02/05/2006		
R/0067	Renewal of the marketing authorisation.	26/01/2006	12/04/2006	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 Prevenar remains positive, but considers that its safety profile should be closely monitored for the reasons indicated below. The remaining safety concerns for Prevenar are fever and febrile reactions, prophylactic antipyretic treatment and vaccine failures. The following adverse reactions should continue to be closely monitored: seizures, hypotonic-hyporesponsive episodes. There is a need to carefully monitor the frequency of pneumococcal infections caused by non-vaccine serotypes. Considering the safety profile of Prevenar and the large number of patients currently enrolled in clinical and post marketing studies for the product as well as the ongoing post-marketing obligations and the continued reports of adverse reactions, the safety profile will continue to be monitored closely and updates will be provided regularly to the CHMP through 2-yearly PSURs. Therefore, based on the safety profile of Prevenar, the CHMP concluded that the MAH should submit one additional

					renewal application for Prevenar in 5 years time.
II/0069	Update of or change(s) to the pharmaceutical documentation	23/03/2006	28/03/2006		
IA/0071	IA_16_b_Submission of new TSE certificate relating to active substance - other substances	26/01/2006	n/a		
II/0066	To amend section 4.5 of the Summary of Product Characteristics to include data on concomitant administration of Prevenar and Meningococcal group C conjugate vaccines. Update of Summary of Product Characteristics	15/09/2005	27/10/2005	SmPC	This variation has been requested by the CHMP in the light of a publication on interactions between the pneumococcal and the meningococcal compound in an experimenatal combination vaccine (Buttery JP, et al: Immunogenicity and safety of a combination pneumococcal-meningococcal vaccine in infants: a randomized controlled trial. JAMA. 2005 Apr 13; 293(14): 1751-8). Information regarding concomitant administration of Prevenar with Meningococcal group C conjugate vaccines is now introduced and was based on data from studies with experimental 9-valent Pneumococcal- Meningococcal combination vaccines.
II/0063	Change(s) to the test method(s) and/or specifications for the active substance	15/09/2005	23/09/2005		
IB/0065	IB_38_b_Change in test procedure of finished product - minor change, biol. active subst./excipient	28/06/2005	n/a		
IB/0064	IB_25_a_01_Change to comply with Ph. - compliance with EU Ph. - active substance	28/06/2005	n/a		
II/0062	Change(s) to the test method(s) and/or specifications for the active substance	26/05/2005	01/06/2005		

IB/0060	IB_12_a_Change in spec. of active subst./agent used in manuf. of active subst. - tightening	05/04/2005	n/a		
II/0056	Change(s) to the test method(s) and/or specifications for the active substance	17/02/2005	24/02/2005		
II/0054	Change(s) to the test method(s) and/or specifications for the active substance	17/02/2005	24/02/2005		
N/0061	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	17/02/2005	n/a	Annex II and PL	
II/0052	To update section 5.1of the SPC to include the results of a clinical trial concerning the Swedish vaccination schedule, supporting a 3-dose schedule between 3 and 12 months of age. Update of Summary of Product Characteristics	15/12/2004	26/01/2005	SmPC and Annex II	This type II variation introduced one information that the Swedish vaccination schedule (3 vaccinations at 3, 5 and 12 months of age) is an acceptable alternative. It was based on data from a study about the immunogenicity induced by Prevenar in children vaccinated according to the current Swedish vaccination program.
IB/0057	IB_23_a_Change in source of excip./reagent to veg./synthetic material - biological act. subst.	11/01/2005	n/a		
IA/0059	IA_12_a_Change in spec. of active subst./agent used in manuf. of active subst. - tightening of spec.	10/01/2005	n/a		
II/0050	Change(s) to the test method(s) and/or specifications for the finished product	15/12/2004	21/12/2004		
II/0036	Update of or change(s) to the pharmaceutical documentation	15/12/2004	21/12/2004		
IA/0058	IA_05_Change in the name and/or address of a manufacturer of the finished product	20/12/2004	n/a	Annex II	

II/0048	Change(s) to the manufacturing process for the active substance	18/11/2004	22/11/2004		
IB/0053	IB_12_a_Change in spec. of active subst./agent used in manuf. of active subst. - tightening	05/11/2004	n/a		
IA/0055	IA_26_a_Change in the specification of immediate packaging - tightening of specification limits	28/10/2004	n/a		
II/0042	Change(s) to the test method(s) and/or specifications for the active substance	16/09/2004	22/09/2004		
II/0041	Change(s) to the test method(s) and/or specifications for the active substance	16/09/2004	22/09/2004		
IB/0047	IB_38_b_Change in test procedure of finished product - minor change, biol. active subst./excipient	09/09/2004	n/a		
II/0038	Quality changes	29/07/2004	02/08/2004		
II/0037	Change(s) to the manufacturing process for the active substance	29/07/2004	02/08/2004		
II/0033	Change(s) to the manufacturing process for the active substance	29/07/2004	02/08/2004		
II/0032	Change(s) to the test method(s) and/or specifications for the active substance	29/07/2004	02/08/2004		
II/0031	Quality changes	29/07/2004	02/08/2004		

II/0018	Extension of Indication	23/06/2004	02/08/2004	SmPC and PL	
IB/0046	IB_12_a_Change in spec. of active subst./agent used in manuf. of active subst. - tightening	30/07/2004	n/a		
IA/0049	IA_28_Change in any part of primary packaging material not in contact with finished product	21/07/2004	n/a		
IA/0045	IA_28_Change in any part of primary packaging material not in contact with finished product	09/07/2004	n/a		
IA/0044	IA_43_a_01_ Add./replacement/del. of measuring or administration device - addition or replacement	09/07/2004	n/a		
II/0029	Change(s) to the manufacturing process for the active substance	23/06/2004	01/07/2004		
II/0026	Change(s) to the test method(s) and/or specifications for the finished product	23/06/2004	01/07/2004		
IA/0040	IA_38_a_Change in test procedure of finished product - minor change to approved test procedure	23/06/2004	n/a		
IA/0035	IA_05_Change in the name and/or address of a manufacturer of the finished product	24/05/2004	n/a	Annex II	
IA/0034	IA_04_Change in name and/or address of a manuf. of the active substance (no Ph. Eur. cert. avail.)	24/05/2004	n/a	Annex II	
II/0019	Change(s) to the test method(s) and/or specifications for the active substance	22/04/2004	27/04/2004		

IA/0030	IA_43_a_01_ Add./replacement/del. of measuring or administration device - addition or replacement	15/04/2004	n/a		
IB/0025	IB_12_a_Change in spec. of active subst./agent used in manuf. of active subst. - tightening	18/02/2004	n/a		
IB/0024	IB_12_a_Change in spec. of active subst./agent used in manuf. of active subst. - tightening	18/02/2004	n/a		
IB/0022	IB_12_a_Change in spec. of active subst./agent used in manuf. of active subst. - tightening	18/02/2004	n/a		
IB/0021	IB_12_a_Change in spec. of active subst./agent used in manuf. of active subst. - tightening	18/02/2004	n/a		
IB/0020	IB_12_a_Change in spec. of active subst./agent used in manuf. of active subst. - tightening	18/02/2004	n/a		
II/0008	Update of Summary of Product Characteristics	22/05/2003	16/09/2003	SmPC	
I/0016	20_Extension of shelf-life as foreseen at time of authorisation	11/07/2003	11/08/2003	SmPC	
I/0014	24a_Change in test procedure for starting material/intermediate used in manuf. of active substance	30/07/2003	05/08/2003		
I/0013	17_Change in specification of the medicinal product	06/06/2003	10/06/2003		
II/0012	Change(s) to the test method(s) and/or specifications for the active substance	22/05/2003	28/05/2003		

II/0009	Update of Summary of Product Characteristics and Package Leaflet	19/09/2002	06/12/2002	SmPC and PL	
I/0011	20_Extension of shelf-life as foreseen at time of authorisation	23/09/2002	17/10/2002	SmPC	
I/0010	20a_Extension of shelf-life or retest period of the active substance	26/09/2002	08/10/2002		
I/0007	12a_Change in specification of starting material/intermediate used in manuf. of the active substance	25/06/2002	28/06/2002		
II/0005	Update of Summary of Product Characteristics	20/09/2001	19/02/2002	SmPC	
II/0003	New presentation(s)	26/07/2001	29/01/2002	SmPC, Labelling and PL	
II/0002	New presentation(s)	26/07/2001	29/01/2002	SmPC, Labelling and PL	
II/0004	Update of Summary of Product Characteristics	23/08/2001	28/01/2002	SmPC	
N/0006	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	07/11/2001	28/02/2002	PL	
II/0001	New presentation(s)	26/04/2001	06/08/2001	SmPC, Labelling and PL	