STEPS TAKEN AFTER GRANTING THE MARKETING AUTHORISATION

For procedures finalised after 1 August 2003 please refer to module 8B.

- The MAH submitted to the EMEA on 7 April 1997 an application for a Type I variation No 12 of Annex I, (Type II procedure applicable) minor change of manufacturing process of the active substance, pursuant to Article 4 of Commission Regulation (EC) No. 542/95 of 10 March 1995. The procedure started on 18 April 1997 and a positive opinion was adopted by the CPMP on 18 June 1997.
- The MAH submitted to the EMEA on 18 April 1997 an application for a Type I variation No 12 of Annex I, (Type II procedure applicable) minor change of manufacturing process of the active substance. The procedure started on 18 April 1997 and a positive opinion was adopted by the CPMP on 18 June 1997.
- The MAH submitted to the EMEA on 4 June 1997 an application for the transfer of the Marketing Authorisation to Hoechst Marion Roussel Deutschland GmbH Germany, pursuant to Article 3 of Commission Regulation (EC) No. 2141/96 of 7 November 1996. The procedure started on 4 June 1997 and a positive opinion was signed by the Executive Director at the EMEA on 6 June 1997.
- The MAH submitted to the EMEA on 27 May 1997 an application for a Type I variation No 11 of Annex I, (Type II procedure applicable) change of manufacturer of the active substance, pursuant to Article 4 of Commission Regulation (EC) No. 542/95 of 10 March 1995. The procedure started on 30 May 1997 and a positive opinion was adopted by the CPMP on 18 June 1997.
- The MAH submitted to the EMEA on 27 May 1997 an application for a Type I variation No 1 of Annex I, change of the Manufacturer responsible for batch release, pursuant to Article 4 of Commission Regulation (EC) No. 542/95 of 10 March 1995. The procedure started on 28 May 1997 and a positive opinion was adopted by the CPMP on 6 June 1997.
- The MAH submitted to the EMEA on 4 June 1997 an application for a Type I variation No 1 of Annex I, (Type II procedure applicable) change of manufacturer responsible for filling, lyophilisation and packaging, pursuant to Article 4 of Commission Regulation (EC) No. 542/95 of 10 March 1995. The procedure started on 9 June 1997 and a positive opinion was adopted by the CPMP on 17 June 1997.
- The MAH submitted to the EMEA on 1 July 1997 an application for a Type I variation, minor change in the manufacture of the medicinal product, consisting of:
  - the use of a newly installed separated filling cabin
  - a new lyophiliser of equivalent make to the previous one in reconstructed building H69
  - the use of "ultraclean" rubber stoppers of the same type supplied by the same manufacturer.

  The variation relates to Article 4 of Commission Regulation (EC) No. 542/95 of 10 March 1995. The procedure started on 25 July 1997 and a positive opinion was adopted by the CPMP on 24 September 1997.
- The MAH submitted to the EMEA on 1 July 1998 an application for a Type II variation for an additional fill size (20 mg, 0.4 ml filled volume) in addition to the already approved fill size, pursuant to Article 6 of Commission Regulation (EC) No. 542/95 of 10 March 1995. The procedure started on 24 July 1998 and a positive opinion was adopted by the CPMP on 17 September 1998.

Subsequent post Marketing Authorisation applications agreed upon are summarised in the table below:

Scope	Application number	Type of modification[1]	Notification/ Opinion issued on[2]	Commission Decision Issued/amended on
Quality changes	II/0010	II	26.04.01	11.05.01
Change in the name of a manufacturer of the active substance	I/0011	I	31.08.01	19.10.01
Changes in the SPC (4.2, 4.3, 4.4, 4.5 and 4.8), Labelling and PL as requested by the CPMP following the assessment of the 5th PSUR.	I/0012	II	18.10.2001	06.02.02
Change in the name and/or address of the marketing authorisation holder, from Hoechst Marion Roussel Deutschland GmbH to Aventis Pharma Deutschland GmbH.	I/0013	I	03.10.01	20.11.01
Renewal	R/0014	R	17.01.02	25.04.02
Transfer of Marketing Authorisation Holder	T/0015	T	21.12.01	19.02.02
Urgent Safety Restriction to warn about the risk of anaphylaxis and precautions for re-exposure	-	USR	-	-
Update of Summary of Product Characteristics and Package Leaflet	II/0016	II	25.04.03	14.07.03
Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	N/0017	N	03.04.03	12.05.03

[1] In accordance with Commission Regulation (EC) No. 542/95 of 10 March 1995, as amended: **I** refers to a minor variation (Type I variation); **II** refers to a major variation (Type II variation); **I/II** refers to a minor variation following the procedure set out in Article 6, 7 and 8 of the Regulation; **X** refers to an Annex II application.
T refers to a transfer of a Marketing Authorisation in accordance with Commission Regulation (EC) No 2141/96 of 7 November 1996.
N refers to a notification in accordance with Article 10(3) of Council Directive 92/27/EEC of 31 March 1992.

[2] For Notifications and Type I variations, the date of entry into force of the change is the EMEA Notification date. The Commission Decision will be amended accordingly.