STEPS TAKEN AFTER GRANTING THE MARKETING AUTHORISATION

For procedures finalised after 1 February 2004 please refer to module 8B.

- The MAH submitted to the EMEA on 11 May 1998 an application for the transfer of the Marketing Authorisation from Novartis Europharm Limited UK to Rhône-Poulenc Rorer S.A. France, pursuant to Article 3 of Commission Regulation (EC) No. 2141/96 of 7 November 1996. The procedure started 26 May 1998. A positive opinion was signed by the Executive Director at the EMEA on 11 June 1998 and forwarded to the European Commission, which adopted a decision on 5 June 1998. (EMEA/H/C/104/I/01)
- The MAH submitted on 11 May 1998 an application for a Type I variation No 1 of Annex I, change in the content of the manufacturing authorisation, pursuant to Article 4 of Commission Regulation (EC) No 542/95 of 10 March 1995. The procedure started on 26 May 1998. The Head of Human Medicines Evaluation Unit at the EMEA signed a positive notification on 11 June 1998. (EMEA/H/C/104/T/02)
- The MAH submitted on 21 June 1999 a notification to the EMEA in order to introduce changes to the Package Leaflet not connected to the Summary of Product Characteristics, pursuant Article 10(3) of Council Directive No. 92/27/EEC of 31 March 1992. The procedure started on 1 December. The notification was signed by the Head of Human Medicines Evaluation Unit on 7 December 1998 and forwarded to the European Commission, which adopted a decision on 26 January 1999. (EMEA/H/C/104/N/03)
- The MAH submitted to the EMEA on 26 November 1998 application for a Type I variation, extension of shelf-life of the finished product, pursuant to Article 4 of Commission Regulation (EC) No 542/95 of 10 March 1995. The procedure started on 3 December 1998. A positive notification was signed by the Head of Human Unit at the EMEA on 17 December 1998 and forwarded to the European Commission, which adopted a decision on 12 March 1999. (EMEA/H/C/104/I/04)
- The MAH submitted to the EMEA on on 9 July 1999 application for a Type I variation, a change of site for secondary packaging is sought through this application, pursuant to Article 4 of Commission Regulation (EC) No 542/95 of 10 March 1995, as amended. The procedure started on 14 July 1999. A positive notification was signed by the Head of Human Unit at the EMEA 28 July 1999 and forwarded to the European Commission, which adopted a decision on 29 July 1999. (EMEA/H/C/104/I/05)
- The MAH submitted to the EMEA on 16 December 1999 applications for a Type I variation, a change in analytical method for the biological assay of the active substance in bulk. This change is accompanied by a consequential change in specification of the bulk active, pursuant to Article 4 of Commission Regulation (EC) No 542/95 of 10 March 1995, as amended. The procedure started on 21 January 2000. A positive opinion was adopted by the CPMP 15 March 2000. (EMEA/H/C/104/I/06) The same change has been submitted for the finished product (EMEA/H/C/104/I/07).
- The MAH submitted to the EMEA on 10 April 2000 application for a Type II variation, a change in the specification of the solvent, water for injection, pursuant to Article 6 of Commission Regulation (EC) No 542/95 of 10 March 1995, as amended. The procedure started on 14 April 2000. A positive opinion was adopted by the CPMP 26 July 2000 and forwarded to the European Commission, which adopted a decision on 2 August 2000. (EMEA/H/C/104/II/08)
- The MAH submitted to the EMEA on 10 May 2000 application for a Type I variation change in the name of the Marketing Authorisation Holder from Rhône-Poulenc Rorer S.A. to Aventis Pharma S.A, pursuant to Article 4 of Commission Regulation (EC) No 542/95 of 10 March 1995, as amended. The MAH, with the submission of this variation updated the EU local representatives in the PL. The procedure started on 17 May 2000. A positive notification was signed by the Head of Head of the Biologicals and Biotechnology sector in the Unit for the

Evaluation of Medicines for Human Use at the EMEA 16 June 2000 and forwarded to the European Commission which adopted a decision on 1 August 2000. (EMEA/H/C/104/I/09)

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
Revision of sections 4.2, 4.4, 4.5, 4.8 of the SPC	II/010	II	19.10.00	22.01.01
5years renewal	R/011	R	25.05.02	02.08.02
Update of Summary of Product Characteristics and Package Leaflet	II/12	II	25.09.03	27.01.04
Change in test procedure of active substance	I/14	I	26.06.03	01.07.03
Change in test procedures of the medicinal product	I/15	I	26.06.03	01.07.03

[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.