PROCEDURAL STEPS TAKEN AFTER GRANTING THE MARKETING AUTHORISATION

For procedures finalised after 01 October 2003, please refer to module 8B

- The MAH submitted to the EMEA on 12 July 1999 application for a Type I variation, a minor change of the manufacturing process of the active substance. Pursuant to Article 4 of Commission Regulation (EC) No 542/95 of 10 March 1995, as amended. The procedure started on 30 July 1999. A positive opinion was adopted by the CPMP 20 October 1999. (EMEA/H/C/232/I/01)
- The MAH submitted on 21 September 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 21 September 1999. The notification was signed by the Head of Human Medicines Evaluation Unit on 18 October 1999 and forwarded to the European Commission which adopted a decision on 31 January 2000. (EMEA/H/C/232/N/02)
- The MAH submitted to the EMEA on 30 September 1999 application for a Type I variation, replacement of bovine-derived excipient with a comparable vegetable-derived excipient, pursuant to Article 4 of Commission Regulation (EC) No 542/95 of 10 March 1995. The procedure started on 4 October 1999. A positive notification was signed by the Head of Human Unit at the EMEA on 18 October 1999. and the European Commission which adopted a decision on 21 October 1999. (EMEA/H/C/232/I/03)
- The MAH submitted to the EMEA on 11 January 2000 an application for a Type I variation, a change of specification of active substance, pursuant to Article 4 of Commission Regulation (EC) No 542/95 of 10 March 1995, as amended. The procedure started on 18 January 2000. A positive notification was signed by the Head ofby the Head of the Biologicals and Biotechnology sector in the Unit for the Evaluation of Medicines for Human Use at the EMEA 16 February 2000 and the European Commission which adopted a decision on 1 March 2000. (EMEA/H/C/232/I/04)
- The MAH submitted on 26 January 2000 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 2 February 2000. The notification was signed by Head of the Biologicals and Biotechnology sector in the Unit for the Evaluation of Medicines for Human Use at the EMEA on 17 February 2000 and forwarded to the European Commission which adopted a decision on 6 April 2000. (EMEA/H/C/232/N/05)
- The MAH submitted to the EMEA on June 2000 application for a Type I variation change following modifications to the manufacturing authorisation in order to apply Wyeth Laboratories, UK as the manufacturing responsible for the batch release and to replace the current one, pursuant to Article 4 of Commission Regulation (EC) No 542/95 of 10 March 1995, as amended. The procedure started on 14 June 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 on 27 June 2000 and forwarded to the European Commission which adopted a decision on 11 August 2000. (EMEA/H/C/232/I/06)

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
Change in the name and/or address of the marketing authorisation holder	I/07	I	06.10.00	27.12.00
Change in pack size for a medicinal product	I/08	I	12.12.00	
Update of or change(s) to the pharmaceutical documentation	II/09	II	23.08.01	03.09.01
Quality changes	II/010	II	18.10.01	31.10.01
Addition of a manufacturing facility and two fold scale-up of purification process	II/012	II	17.01.02	23.01.02
Additional drug product facility	II/013	II	17.01.02	23.01.02
Update of the SPC (point 4.8)	II/014	II	21.02.02	25.06.02
Compliance with Core SPC for human plasma	II/015	II	24.04.02	20.08.02
Change in supplier of an intermediate compound used in manufacture of the active substance	I/016	I	29.10.01	31.10.01
Change in the name of manufacturer	I/020	I	29.01.02	28.02.02
New stopper for sodium chloride diluent	II/021	II	24.04.02	29.04.02
Line Extension	X/022	X	19.09.02	19.12.02
Scale-up of MAb sepharose chromatography resin coupling process	II/023	II	21.11.02	10.12.02
Elimination of amino acid analysis testing on incoming KGSF 14 media	II/024	II	17.10.02	21.10.02
Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	N/025	N	23.08.02	18.09.02
Quality changes	II/026	II	20.02.03	08.05.03
Change(s) to the test method(s) and/or specifications for the active substance	II/027	II	20.03.03	26.03.03
Transfer of Marketing Authorisation Holder	T//028	T	31.03.03	15.05.03
Change in or addition of manufacturing site(s) for part or all of the manufacturing process and Change in the name of a manufacturer of the active substance	I/029	I	18.07.03	22.07.03
Minor change of manufacturing process of the active substance	I/030	I	25.09.03	02.10.03
Extension of shelf-life or retest period of the active substance	I/035	I	22.09.03	23.09.03

[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.