Steps taken after granting the Marketing Authorisation

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

- The MAH submitted on 22 April 1999, an application for a Notification of a Type I variation No 20 of Annex I, in order to change the shelf-life of the finished product from 12 to 18 months, pursuant to Article 4 of Commission Regulation (EC) No 542/95 of 10 March 1995 as amended. The procedure started on 30 April 1999. The positive notification was signed by the Head of Human Medicines Evaluation Unit at the EMEA on 26 May 1999 (EMEA/H/C/207/I/01) and forwarded to the European Commission which amended the Commission Decision on 29 July 1999.

- The MAH submitted on 6 April 1998, an application for a Notification of a Type I variation No 20 of Annex I, in order to change the shelf-life of the active substance from 6 to 12 months, pursuant to Article 4 of Commission Regulation (EC) No 542/95 of 10 March 1995 as amended. The procedure started on 30 April 1999. The positive notification was signed by the Head of Human Medicines Evaluation Unit at the EMEA on 26 May 1999 (EMEA/H/C/207/I/02) and was forwarded to the European Commission.

- The MAH submitted on 22 April 1999, an application for two Type I variations No 24 and a Type I variation No 14 with a consequential variation No 17 of Annex I, (type II procedure applicable) in order to change the specifications and test procedures of the active substance and medicinal product, pursuant to Article 4 of Commission Regulation (EC) No 542/95 of 10 March 1995 as amended. The procedures started on 26 April 1999 and positive opinions were adopted by the CPMP on 24 June 1999 (EMEA/H/C/207/I/03-05) and forwarded to the European Commission, which amended the Commission Decision on 22 September 1999.

- The MAH submitted on 6 April 1999, a Notification to the EMEA in order to introduce changes to the Package Leaflet not connected to the Summary of Product Characteristics, pursuant to Article 10(3) of Council Directive No. 92/27/EEC of 31 March 1992. The procedure started on 30 April 1999. The positive Notification was signed by the Head of Human Medicines Evaluation Unit at the EMEA on 26 May 1999 (EMEA/H/C/207/N/06). The European Commission amended the annexes to the Commission Decision on 29 July 1999.

- The MAH submitted on 11 October 1999, an application for a Notification of a Type I variation No 20 of Annex I, in order to extend the self-life of the medicinal product, pursuant to Article 4 of Commission Regulation (EC) No 542/95 of 10 March 1995 as amended. The procedure started on 15 October 1999. A positive Notification was signed by the Head of Human Unit at the EMEA on 12 November 1999 (EMEA/H/C/207/I/07) and forwarded to the European Commission, which amended the Commission Decision on 8 February 2000.

- The MAH submitted on 11 October 1999, an application for a Type I variation No 20a of Annex I, in order to extend the shelf-life or re-test period 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 15 October 1999. A positive opinion was signed by the Head of Human Unit at the EMEA on 12 November 1999 (EMEA/H/C/207/I/08) and forwarded to the European Commission, which amended the Commission Decision on 15 December 1999.

- The MAH submitted on 21 September 1999, an application for a Type I variation No 1 and two consequential application for Type I variations, Nos 15 and 16 of Annex I, (type II procedure applicable) in order to change the content of the manufacturing authorisation, the manufacture of the medicinal product and the batch size of the finished product, pursuant to Article 4 of Commission Regulation (EC) No 542/95 of 10 March 1995 as amended. The procedure started on 22 October 1999 and a positive opinion was adopted by the CPMP on 16 February 2000 (EMEA/H/C/207/I/09) and forwarded to the European Commission, which amended the Commission Decision on 17 May 2000.

- The MAH submitted on 3 December 1999, an application for two Type I variations No 24 of Annex I, (type II procedure applicable) in order to change test procedure of active substance, pursuant to Article 4 of Commission Regulation (EC) No 542/95 of 10 March 1995 as amended. The procedure started on 17 December 1999 and a positive opinion was adopted by the CPMP on 16 February 2000 (EMEA/H/C/207/I/10-11) and forwarded to the European Commission, which amended the Commission Decision 17 May 2000.

- The MAH submitted on 3 December 1999, an application for a Type I variation No 25 of Annex I, (type II procedure applicable) in order to change the test procedures of the medicinal product, pursuant to Article 4 of Commission Regulation (EC) No 542/95 of 10 March 1995 as amended. The procedure started on 17 December 1999 and a positive opinion was adopted by the CPMP on 16 February 2000 (EMEA/H/C/207/I/12) and forwarded to the European Commission, which amended the Commission Decision on 17 May 2000.

- The MAH submitted on 3 February 2000 an application for a Type II variation at the request of the CPMP following the evaluation of the 3rd PSUR, in order to modify the SPC and Package Leaflet, pursuant to Article 6 of Commission Regulation (EC) No 542/95 of 10 March 1995 as amended. The procedure started on 18 February 2000 and a positive opinion was adopted by the CPMP on 12 April 2000. The European Commission granted a Commission Decision on 11 July 2000 (EMEA/H/C/207/II/13).

- The MAH submitted on 28 March 2000 an application for a Type II variation, in order to extend the current indication of Simulect to paediatric patients, pursuant to Article 6 of Commission Regulation (EC) No 542/95 of 10 March 1995. The procedure started on 14 April 2000, supplementary information was supplied by the MAH on 11 July 2000 and a positive opinion was adopted by the CPMP on 26 July 2000 (EMEA/H/C/207/II/14). The European Commission granted a Commission Decision on 1 December 2000.

- The MAH submitted on 28 March 2000 an application for a Type II variation, in order to use Simulect together with a triple immunosuppression, pursuant to Article 6 of Commission Regulation (EC) No 542/95 of 10 March 1995. The procedure started on 14 April 2000, supplementary information was supplied by the MAH on 11 July 2000 and a positive opinion was adopted by the CPMP on 26 July 2000 (EMEA/H/C/207/II/15). The European Commission granted a Commission Decision on 1 December 2000.

- The MAH submitted on 28 March 2000 an application for a Type II variation, for an additional method of administration (iv bolus injection), pursuant to Article 6 of Commission Regulation (EC) No 542/95 of 10 March 1995. The procedure started on 14 April 2000, supplementary information was supplied by the MAH on 11 July 2000 and a positive opinion was adopted by the CPMP on 26 July 2000 (EMEA/H/C/207/II/16). The European Commission granted a Commission Decision on 1 December 2000.

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

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

Scope	Application number	Type of modification[1]	Notification/ Opinion issued on[2]	Commission Decision Issued/amended on
Extension of shelf-life or retest period of the active substance.	I/0017	I	25.01.01	05.02.01
Extension of shelf-life as foreseen at time of authorisation.	I/0018	I	25.01.01	26.03.01
Change following modification(s) of the manufacturing authorisation(s).	I/0019	I	25.01.01	05.02.01
Minor change of manufacturing process of the active substance.	I-0020	I	15.11.01	27.02.02
Minor change of manufacturing process of active substance.	I-0021	I	15.11.01	27.02.02
Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification).	N/0022	N	21.01.02	02.04.02
Change following modification(s) of the manufacturing authorisation(s). Minor changes in manufacture of the medicinal product.	I/0023	I	18.10.01	
Changes to comply with supplements to pharmacopoeias.	I/0024	I	18.10.01	-
Changes to comply with supplements to pharmacopoeias.	I/0025	I	18.10.01	-
Centralised line extension for the new strength (10 mg) of Simulect, initially approved in 20 mg dosage strength.	X-0026	Annex II application	21.11.02	07.03.02
Changes to comply with supplements to pharmacopoeias.	I-0027	I	21.08.02	-
Change(s) to the test method(s) and/or specifications for the active substance.	II-0028	II	17.10.02	25.10.02
Change(s) to the test method(s) and/or specifications for the finished product.	II-0029	II	19.09.02	25.09.02
Changes in sections 4.4, 4.8 and 5.1 of the SPC to include the long-term data of the pivotal studies CHIB 201-E-01 and CHIB 352-E-01 (particularly the five year safety and the general efficacy, further to the request of the CPMP on June 2002). Moreover, inclusion of QRD comments to the SPC, PL and Labelling as previously in Simulect 10mg line extension. In addition, inclusion of minor corrections in section 4.8 of both strengths in line with the Core Data Sheet. Finally, inclusion of linguistic corrections to the Italian 20mg strengths SPC and PL.	II-0031	II	20.02.03	23.05.03
Change in the name of the Manufacturing Authorisation Holder responsible for the batch release.	I-0032	I	15.04.03	04.06.03
Renewal of the Marketing Authorisation	R-033	R	24.07.03	20.10.03
Minor change to the package leaflet not connected to the SPC, to include the local representatives of the MAH for all 10 new European Member States, to change the contact details for all local representatives to include only the company name and telephone number in accordance with the latest EMEA/QRD template, and the change of contact for Iceland. (Art. 61.3 Notification)	N-034	N	03.05.04	-

[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.