STEPS TAKEN AFTER GRANTING THE MARKETING AUTHORISATION

For procedures finalised after 01 December 2001 please refer to module 8B**.**

- On 8 November 1999, the Marketing Authorisation Holder (MAH) submitted an application for a Type I variation (I/01) in accordance with Commission Regulation (EC) No. 542/95. The MAH applied for a minor change of manufacturing process of the active substance. On 16 December 1999 the EMEA approved the variation, which did not lead to any changes to the Commission Decision.
- In accordance with Article 10(3) of Council Directive 92/27/EEC of 31 March 1992, the EMEA issued on 19 December 1999 a Notification for amendment of the addresses of the local representatives mentioned in the Package Leaflet, and some aspects of the Labelling, as applied by the MAH. (N/02)
- On 9 March 2000, the MAH submitted an application for a type I variation (I/03) in accordance with Commission Regulation (EC) 542/95 as amended, related to a change in test procedures of the medicinal product. On 6 April 2000 the EMEA approved the variation, which did not lead to any changes to the Commission Decision.
- On 9 March 2000, the MAH submitted in parallel three applications for type I variations (I/04, 05, & 06) in accordance with Commission Regulation (EC) 542/95 as amended, related to a change in test procedures of the medicinal product. On 25 May 2000 the EMEA approved the variations, which did not lead to any changes to the Commission Decision.
- On 9 March 2000, the MAH submitted an application for a type I variation (I/07) in accordance with Commission Regulation (EC) 542/95 as amended, related to the deletion of the alternative site for packaging of the finished product. On 6 April 2000 the EMEA approved the variation, which did not lead to any changes to the Commission Decision.
- On 22 April 1999 the MAH submitted an application for a Type II variation, (II/08) in accordance with Commission Regulation (EC) No. 542/95, as amended. The Marketing Authorisation Holder applied for a modification of the shelf life specifications of the finished product, namely to widen the shelf life limits for the active ingredient. The CPMP adopted on 21 September 2000 an Opinion on the Type II variation, which did not lead to any changes to the Commission Decision.
- In accordance with Article 10(3) of Council Directive 92/27/EEC of 31 March 1992, the EMEA issued on 9 June 2000 a Notification for amendment of the addresses of the local representatives mentioned in the Package Leaflet, as applied by the MAH. (N/09).
- On 26 September 2000, the MAH submitted in parallel two applications for type I variations (I/10 and I/11) in accordance with Commission Regulation (EC) 542/95 as amended, related to the replacement of an excipient with a comparable excipient. On 27 October 2000 the EMEA approved these variations which did not lead to any changes to the Commission Decision.

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
To update the Summary of Product Characteristics (SPC), sections 4.2 "Posology and Method of Administration", 4.4 "Special warnings and special precautions for use", 4.6 "Pregnancy and lactation", 4.8 "Undesirable effects" and 5.3 "Preclinical safety data" and related relevant sections of the Package Leaflet (PL). Furthermore, the Marketing Authorisation Holder (MAH) proposed some minor changes in the SPC, Labelling and PL in order to bring the text in line with the latest QRD/ EMEA templates.	II/0012	II	26.07.01	21.11.01
Change in process controls applied during the manufacture of the product.	I/0013	I	14.05.01	N/A

[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.