Procedural steps taken after granting the Marketing Authorisation

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

- On 15 November 2000 the Marketing Authorisation Holder submitted a Type II Variation in accordance with Commission Regulation (EC) No. 542/95 as amended. This variation was submitted to demonstrate compliance with Commission Directive 1999/82/EC and the Note for Guidance on Minimising the Risk of Transmitting Animal Spongiform Encephalopathy Agents via Medicinal Products (CPMP/BWP/1230/98 rev.1) and provided scientific information, which was then supplemented by a Certificate of Suitability issued by the European Pharmacopoeia. The CPMP, during its March 2001 plenary meeting, considered the variation acceptable and issued on 29 March 2001 an Opinion on the Type II variation to the Commission Decision Authorisation of 29 September 2000, as amended.

- Pursuant to Article 4 of Commission Regulation (EC) No. 542/95 of 10 March 1995 as amended, the MAH submitted to the EMEA on 15 November 2000 an application for a Type I variation for Keppra. The MAH applied to increase product capacity by increasing batch sizes in the synthesis of the active substance. The EMEA notified the European Commission that the above-mentioned variation was acceptable on 20 December 2000.

- Pursuant to Article 4 of Commission Regulation (EC) No. 542/95 of 10 March 1995 as amended, the MAH submitted to the EMEA on 27 November 2000 an application for a Type I variation for Keppra. The MAH applied to update chemical and pharmaceutical documentation concerning manufacturing process of the active substance. The EMEA notified the European Commission that the above-mentioned variation was acceptable on 20 December 2000.
- Pursuant to Article 4 of Commission Regulation (EC) No. 542/95 of 10 March 1995 as amended, the MAH submitted to the EMEA on 27 November 2000 an application for a Type I variation for Keppra. The Marketing Authorisation Holder applied to update the chemical and pharmaceutical documentation in order to increase the batch size of intermediates used in the active substance synthesis. The EMEA notified the European Commission that the above-mentioned variation was acceptable on 20 December 2000.

- Pursuant to Article 4 of Commission Regulation (EC) No. 542/95 of 10 March 1995 as amended, the MAH submitted to the EMEA on 1 December 2000 an application for a Type I variation for Keppra. The Marketing Authorisation Holder applied to include an alternative site for the manufacture of intermediates used in the active substance synthesis. The EMEA notified the European Commission that the above-mentioned variation was acceptable on 22 January 2001.

- Pursuant to Article 4 of Commission Regulation (EC) No. 542/95 of 10 March 1995 as amended, the MAH submitted to the EMEA on 15 December 2000 an application for a Type I variation for Keppra. The Marketing Authorisation Holder applied to include the storage condition ‘do not store above 25°C.’ on the product literature. Minor French linguistic corrections and an address change for a local representative in the package leaflet were proposed. The EMEA notified the European Commission that the above-mentioned variation was acceptable on 2 March 2001. The amended Commission Decision was issued on 27 April 2001.

- Pursuant to Article 4 of Commission Regulation (EC) No. 542/95 of 10 March 1995 as amended, the MAH submitted to the EMEA on 3 January 2001 an application for a Type I variation for Keppra. The Marketing Authorisation Holder applied to increase the batch size for the intermediates of the active substance synthesis. The EMEA notified the European Commission that the above-mentioned variation was acceptable on 22 January 2001.

- Pursuant to Article 4 of Commission Regulation (EC) No. 542/95 of 10 March 1995 as amended, the MAH submitted to the EMEA on 3 January 2001 an application for a Type I variation for Keppra. The Marketing Authorisation Holder applied for a change to the analytical method used for the analysis of a starting material. The EMEA notified the European Commission that the above-mentioned variation was acceptable on 22 January 2001.

- Pursuant to Article 4 of Commission Regulation (EC) No. 542/95 of 10 March 1995 as amended, the MAH submitted to the EMEA on 31 January 2001 applications for three Type I variations for Keppra. The Marketing Authorisation Holder applied for changes to the test procedure for the finished product. The EMEA notified the European Commission that the above-mentioned variations were acceptable on 7 March 2001.

- On 11 April 2001 the Marketing Authorisation Holder submitted a Type II Variation in accordance with Commission Regulation (EC) No. 542/95 as amended. This variation was submitted to introduce a new alternative route of synthesis for the active substance levetiracetam. The CPMP, during its September 2001 plenary meeting, considered the variation acceptable and issued on 20 September 2001 an Opinion on the Type II variation to the Commission Decision Authorisation of 29 September 2000, as amended.

- Pursuant to Article 4 of Commission Regulation (EC) No. 542/95 of 10 March 1995 as amended, the MAH submitted to the EMEA on 18 October 2001 an application for a Type I variation for Keppra. The Marketing Authorisation Holder applied for a change in supplier of an intermediate compound used in the manufacture of the active substance. The EMEA notified the European Commission that the above-mentioned variations were acceptable on 21 November 2001.

- The MAH submitted on 10 January 2002 a request to introduce changes to an aspect of the labelling not connected to the SPC, in accordance with Article 61(3) of Council Directive No 2001/83/EC. This change relates to addition of spaces and writing the abbreviation Exp in lower case instead of capitals. The MAH received a positive notification from the EMEA on 5 February 2002.

- Pursuant to Article 4 of Commission Regulation (EC) No. 542/95 of 10 March 1995 as amended, the MAH submitted to the EMEA on 8 February 2002 an application for a Type I variation for Keppra. The Marketing Authorisation Holder applied for a minor change of manufacturing process of the active substance. The EMEA notified the European Commission that the above-mentioned variations were acceptable on 15 March 2002.

- Pursuant to Article 4 of Commission Regulation (EC) No. 542/95 of 10 March 1995 as amended, the MAH submitted to the EMEA on 11 April 2002 an application for a Type I variation for Keppra. The Marketing Authorisation Holder applied for changes to comply with supplements to pharmacopoeias. The EMEA notified the European Commission that the above-mentioned variations were acceptable on 15 March 2002.

- On 6 November 2001, the Marketing Authorisation Holder submitted an application for a Type II variation in accordance with Art. 6 of Commission Regulation (EC) No. 542/95, as amended. The Marketing Authorisation Holder applied for a variation to update the SPC following assessment of the second PSUR. The CPMP during its April 2002 plenary meeting considered the variation acceptable and issued on 25 April 2002 a positive Opinion on the Type II variation. The corresponding Commission Decision was issued on 18 July 2002.

- Pursuant to Article 4 of Commission Regulation (EC) No. 542/95 of 10 March 1995 as amended, the MAH submitted to the EMEA on 14 August 2002 an application for a Type I variation for Keppra. (EMEA/H/C//277I/21) The Marketing Authorisation Holder applied for a change in supplier of an intermediate compound used in the manufacture of the active substance. The EMEA notified the European Commission that the above-mentioned variations were acceptable on 20 September 2002.

- Pursuant to Article 4 of Commission Regulation (EC) No. 542/95 of 10 March 1995 as amended, the MAH submitted to the EMEA on 3 September 2002 an application for a Type I variation for Keppra. (EMEA/H/C/277/I/22) The Marketing Authorisation Holder applied for an addition of manufacturer of active substance. The EMEA notified the European Commission that the above-mentioned variations were acceptable on 1 October 2002.

- Pursuant to Article 4 of Commission Regulation (EC) No. 542/95 of 10 March 1995 as amended, the MAH submitted to the EMEA on 19 September 2002 an application for a Type I variation for Keppra (EMEA/H/C/277/I/23). The Marketing Authorisation Holder applied for a minor change of manufacturing process of the active substance. The EMEA notified the European Commission that the above-mentioned variations were acceptable on 18 October 2002.

- Pursuant to Article 4 of Commission Regulation (EC) No. 542/95 of 10 March 1995 as amended, the MAH submitted to the EMEA on 03 October 2002 an application for a Type I variation for Keppra (EMEA/H/C/277/I/24). The Marketing Authorisation Holder applied for a change of batch size of active substance. The EMEA notified the European Commission that the above-mentioned variations were acceptable on 25 October 2002.

- On 6 August 2002, the Marketing Authorisation Holder submitted an application for a Type II variation in accordance with Art. 6 of Commission Regulation (EC) No. 542/95, as amended, for a variation to update the SPC following assessment of the 3rd and 4th PSUR. In addition, the opportunity was taken to amend minor typographical errors and better reflect the initial analysis on preclinical safety data (EMEA/H/C/277/II/20). The CPMP during its October 2002 plenary meeting considered the variation acceptable and issued on 17 October 2002 a positive Opinion on the Type II variation. The corresponding Commission Decision was issued on 14 January 2003.

- Pursuant to Article 4 of Commission Regulation (EC) No. 542/95 of 10 March 1995 as amended, the MAH submitted to the EMEA on 18 November 2002 an application for a Type I variation for Keppra (EMEA/H/C/277/I/25). The Marketing Authorisation Holder applied for an extension of shelf life as foreseen at time of authorisation. The EMEA notified the European Commission that the above-mentioned variations were acceptable on 17 January 2003.

- On 5 February 2002, the Marketing Authorisation Holder submitted an application for Marketing Authorisation to the European Agency for the Evaluation of Medicinal Products (EMEA) for Keppra 100 mg/ml Oral Solution under Annex II to Commission Regulation (EC) No. 542/95 as amended (EMEA/H/C/277/X/18). During the meeting on 19-21 November 2002 the CPMP, in the light of the overall data submitted and the scientific discussion within the Committee, issued a positive opinion for granting a Marketing Authorisation to Keppra 100 mg/ml Oral Solution on 21 November 2002. The corresponding Commission Decision was issued on 03 March 2003.

- On 10 December 2002, the Marketing Authorisation Holder submitted an application for a Type II variation in accordance with Art. 6 of Commission Regulation (EC) No. 542/95, as amended, for a variation to add an alternative manufacturing site for the active substance manufacturing process (EMEA/H/C/277/II/26). During the April 2003 meeting, the CPMP, adopted a positive opinion on the variation on 25 April 2003. The corresponding Commission Decision was issued on 02 May 2003.

- Pursuant to Article 4 of Commission Regulation (EC) No. 542/95 of 10 March 1995 as amended, the MAH submitted to the EMEA on 20 June 2003 an application for a Type I variation for the deletion of a colouring agent from the coating formulation used for the 500 mg.film-coated tablets (EMEA/H/C/277/I/27). The EMEA notified the European Commission that this variation was acceptable on 30 July 2003.

- On 16 July 2003 the Marketing Authorisation Holder submitted an application for a Type II variation in accordance with Art. 6 of Commission Regulation (EC) No. 542/95, as amended, for a variation to add an alternative manufacturing site for the active substance manufacturing process (EMEA/H/C/277/II/28). The CPMP, during its November plenary meeting, considered the changes acceptable and issued on 20 November 2003 an Opinion on the Type II variation to the Community Marketing Authorisation. The corresponding Commission Decision was issued on 16 December 2003.