Steps taken after granting the Marketing Authorisation

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

- The MAH submitted on 17 September 1997 two type I variations in accordance with Article 5 of Commission Regulation (EC) No 542/95 [(extension of shelf life from 2 to 3 years EMEA/H/C/132/I/02) and minor changes in the manufacturing process (EMEA/H/C/132/I/01)]. The MAH received a positive notification from the EMEA on 28 October 1997 (type I, no 20, extension of shelf-life) and on 25 November 1997 (type I, no 12, minor change of the manufacturing process of the active substance).

- On 16 February 1998, The MAH submitted an application for a Type I variation (EMEA/H/C/132/I/03) for a change in the content of the manufacturing authorisation (additional Primary Packaging and Batch Release site). The MAH received a positive notification from the EMEA on 24 April 1998 for the Type I Variation application.

- On 20 October 1998 the MAH applied for a Type II variation for Tasmar (EMEA/H/C/132/II/04**)** to update sections 4.2 (Posology and method of administration), 4.4 (Special warnings and special precautions for use), 4.8 (Undesirable effects) and 4.9 (Overdose) of the Summary of Product Characteristics (SPC), and as a consequence the Package Leaflet following new data provisionally introduced through two Urgent Safety Restrictions (USRs). The CPMP, during its October 1998 plenary meeting, considered the changes acceptable and issued on 21 October 1998 a positive Opinion on this Type II variation.

- In the post-opinion phase of variation EMEA/H/C/132/II/04, prior to the variation receiving a Commission Decision, the European Commission requested the Opinion of the EMEA on cases of hepatotoxicity and neuroleptic malignant-like syndrome. On 10 November 1998, the CPMP convened an extraordinary meeting to review the cases. Following that meeting, the CPMP adopted, on 12 November 1998, an Opinion recommending the suspension of the marketing authorisation for Tasmar due to increasing concerns over reports of severe hepatotoxicity, three with a fatal outcome. The European Commission issued a Decision suspending the Marketing Authorisation of Tasmar on 11 December 1998, for the period of one year renewable.

- Subsequently, decisions renewing the suspension of the Tasmar Marketing Authorisation for the period of one year have been issued by the European Commission on 20 January 2000, 29 January 2001, 17 December 2001, 7 January 2003 and 14 January 2004, following the CPMP opinions dated 21 October 1999, 19 October 2000, 19 September 2001, 19 September 2002 and 22 October 2003, respectively.

- Although on 22 October 2003, the CPMP adopted an Opinion recommending the renewal of the suspension of the marketing authorisation for Tasmar, for a further year, the CPMP agreed on a list of outstanding issues to be addressed by the MAH focussing on the submission of revised product information and proposals for safety measures relating to the possible re-introduction of Tasmar into the EU market.

- Therefore, on 16 February 2004, the MAH submitted documentation to support their request for the lifting of the suspension of the Marketing Authorisation for Tasmar addressing the issues raised by CPMP during its October 2003 plenary meeting, including a proposal to ensure safe use of Tasmar, a communication plan to prescribers including a Dear Doctor Letter and a revised Product Information. During its April 2004 plenary meeting, the CPMP adopted on 22 April 2004 an Opinion recommending the lifting of the suspension of the Marketing Authorisation for Tasmar. The MAH provided the letter of undertaking on the measures to be fulfilled further to the lifting of the suspension on 22 April 2004.