STEPS TAKEN AFTER GRANTING THE MARKETING AUTHORISATION

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

- On 30 March 2000 the MAH (MAH) submitted to the EMEA an application for a Type I variation in accordance with Commission Regulation (EC) No. 542/95 of 10 March 1995, as amended. The scope of this variation was to change the name of the manufacturer of the finished product from Circa Pharmaceuticals Inc. to Watson Laboratories Inc. This variation was approved by the EMEA on 28 April 2000 and did not require any amendments to the Commission Decision.
- On 30 March 2000 the MAH submitted to the EMEA an application for a Type II variation in accordance with Commission Regulation (EC) No. 542/95 of 10 March 1995, as amended. The scope of this variation was to add an alternative active substance manufacturer Genzyme Ltd, Haverhill, Suffolk, UK and to resubmit the originally open file information of the active substance manufacturing process at the Dow Chemical Company site as an open/closed European Drug Master File (EDMF). The CPMP adopted a positive opinion for this variation on 21 September 2000, which did not require any amendments to the Community Marketing Authorisation.
- On 30 March 2000, the MAH submitted an application for a marketing authorisation for Renagel film coated tablets, in accordance with Annex II to Commission Regulation (EC) No 542/95 as amended. The procedure started on 14 April 2000. During its December 2000 meeting, the CPMP, in light of the overall data submitted and the scientific discussion within the CPMP issued a positive opinion for granting a Marketing Authorisation for Renagel 400 mg film coated tablets and Renagel 800 mg film coated tablets on 14 December 2000. The CPMP opinion was forwarded to the European Commission, which adopted the corresponding Decision on 26 March 2001.
- On 10 January 2001, the MAH applied for a Type I variation for Renagel hard capsules, in accordance with Commission Regulation (EC) 542/95 as amended. Additional data was submitted on 1 February 2001. The MAH applied to demonstrate compliance with the 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), and provided certificates of suitability issued by the European Pharmacopoeia. The EMEA considered this variation to be acceptable and issued on 2 March 2001 a positive notification for the Type I variation application.
- On 20 February 2001, the MAH submitted an application for a Type II variation in accordance with Article 6 of European Commission Regulation (EC) 542/95 as amended. The MAH applied for an update of the section 4.8 of the SPC and PL to include flatulence based on the 1st PSUR. Some minor linguistic corrections were also applied for. The CPMP adopted a positive Opinion for this variation on 26 April 2001. The respective Commission Decision was issued on 9 August 2001.
- On 14 May 2001 the MAH submitted to the EMEA an application for a Type I variation in accordance with Commission Regulation (EC) No. 542/95 of 10 March 1995, as amended. The scope of this variation was to add a new pack size of 100 tablets for the 800 mg strength. This variation was approved by the EMEA on 22 June 2001. The respective Commission Ddecision was issued on 15 October 2001.
- On 24 August 2001 the MAH submitted to the EMEA an application for a Type I variation in accordance with Commission Regulation (EC) No. 542/95 of 10 March 1995, as amended. The scope of this variation was a minor change in the manufacturing procedure. This variation was approved by the EMEA on 28 September 2001 and did not require any amendments to the Community Marketing Authorisation.

- On 30 October 2001 the MAH submitted to the EMEA an application for a Type I variation in accordance with Commission Regulation (EC) No. 542/95 of 10 March 1995, as amended. The scope of this variation was to change its name from Genzyme B.V. into Genzyme Europe B.V. This variation was approved by the EMEA on 10 December 2001 and did not require any amendments to the Community Marketing Authorisation.

- On 30 October 2001 the MAH submitted to the EMEA an application for a Type I variation in accordance with Commission Regulation (EC) No. 542/95 of 10 March 1995, as amended. The scope of this variation was to upgrade the current seal for the 403 mg capsule bottle to provide better protection against moisture and to be of the same quality as the one used for Renagel 400 mg/800 mg film-coated tablets. This variation was approved by the EMEA on 10 December 2001 and did not require any amendments to the Community Marketing Authorisation.

- On 10 June 2002 the MAH submitted to the EMEA an application for a Type I variation in accordance with Commission Regulation (EC) No. 542/95 of 10 March 1995, as amended. The scope of this variation was a change of the manufacturing site for part or all of the manufacturing process of the medicinal product. The procedure started on 27 June 2002. This variation was approved by the EMEA on 10 July 2002 and did not require any amendments to the Community Marketing Authorisation.

- On 3 September 2002 the MAH submitted to the EMEA an application for a Type I variation in accordance with Commission Regulation (EC) No. 542/95 of 10 March 1995, as amended. The scope of this variation was a change in test procedure of active substance and the medicinal product. The procedure started on 10 September 2002. This variation was approved by the EMEA on 4 October 2002 and did not require any amendment to the Community Marketing Authorisation.