STEPS TAKEN AFTER THE GRANTING OF THE MARKETING AUTHORISATION

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

- On 7 March 2002 the European Commission issued a Decision for a Type I variation (EMEA/H/C/370/I/01) for a change in the name of the Marketing Authorisation Holder (MAH) from Genzyme B.V. to Genzyme Europe B.V.

- On 17 September 2002 the European Commission issued a Decision for a Type I variation (EMEA/H/C/370/I/02), for a change in test procedure of active substance (correction of the concentration of the GZ-14 reference standard used in the IEF and peptide map assays for the active substance release testing).

- On 29 July 2002 the European Commission issued a Decision on a Type II variation (EMEA/H/C/370/II/03) the scope of which was to change the test method and/or specifications for the active substance (revision of the assay method for the detection of protein impurities and mannose-6-phosphate in the active substance).

- On 02 December 2002 the European Commission issued a Decision on a Type II variation (EMEA/H/C/370/II/04) to authorise an additional presentation (5 mg) with the same strength after reconstitution as the already authorised 35 mg presentation.

- On 24 January 2003 the European Commission issued a Decision on the 1st Annual Re-Assessment (EMEA/H/C/370/S/06) of the specific obligations and the benefit/risk ratio. No amendments of Annexes I and III to the Community Marketing Authorisation were necessary. The marketing authorisation for Fabrazyme remained under exceptional circumstances. The list of Specific obligations set out in Annex II was revised according to the conclusions of the CPMP discussion.

- On 08 April 2003 the European Commission issued a Decision on a Type II variation (EMEA/H/C/370/II/05) in order to add a new manufacturing site for the drug substance, and scale up both the drug substance and drug product manufacturing process.

- On 19 May 2003 the European Commission issued a Decision on a Type II variation (EMEA/H/C/370/II/07) relating to an update of the Summary of Product Characteristics (SPC), as a result of an 18-months interim report of the ongoing open label extension phase 3 trial AGAL-005-99, and completion of study 01012 (evaluation of developmental toxicity in rats) and study FB9702-01 (phase 1/2 dose finding). Additionally, CPMP recommendations following assessment of the 1st PSUR were implemented.

- On 22 July 2003 the European Commission issued a Decision on a Type II variation (EMEA/H/C/370/II/08) relating to an update of section 4.8 of the SPC, as requested by CPMP following the assessment of the 2nd PSUR.

- On 05 August 2003 the European Commission issued a Decision on a Type I variation (EMEA/H/C/370/I/09) to extend the shelf life of the finished product.