

PROCEDURAL STEPS TAKEN AFTER THE GRANTING OF THE MARKETING AUTHORISATION

For procedures finalised after 15 October 2003 please refer to module 8B.

On 24 October 2001 the EMEA, following submission of a Type I variation (EMEA/H/C/369/I/01), notified a change in the name of the manufacturer of the active substance from Bio Science Production Corp. to Cambrex Bio Science Inc.

On 13 December 2001 the EMEA, further to the submission of a Type I variation (which followed a Type II procedure: EMEA/H/C/369/I/02), notified a change in test procedure of active substance and consequential changes in specifications of active substance and finished product, within the scope of item No 24 with consequential change no. 14 and 17 of Annex I to Commission Regulation (EC) No 542/95, as amended.

On 17 January 2002 the EMEA, further to the submission of a Type I variation (which followed a Type II procedure: EMEA/H/C/369/I/03) notified a change in test procedure of active substance and consequential changes in specifications of active substance related to host cell proteins, within the scope of item No 24 with consequential change no. 14 of Annex I to Commission Regulation (EC) No 542/95, as amended.

On 17 January 2002 the EMEA, further to the submission of a Type I variation : (EMEA/H/C/369/I/04) concerning a minor change of manufacturing process of the active substance within the scope of item No 12 of Annex I to Commission Regulation (EC) No 542/95, as amended.

On 10 April 2002 the European Commission issued a Decision further to a Marketing Authorisation Holder application to (EMEA/H/C/369/N/05) to introduce a number of minor changes to aspects of Labelling and Package Leaflet not connected to the Summary of Product Characteristics.

On 24 May 2002 the European Commission issued a Decision on a Type II variation application (EMEA/H/C/369/II/06) to update of Part II of the dossier.

On 12 September 2002 the European Commission issued a Decision on a Type II variation (EMEA/H/C/369/II/07) to update the Part II of the dossier.

On 10 September 2002, the European Commission issued a Decision on two applications for Type I variations (EMEA/H/C/369/I/09 and EMEA/H/C/369/I/10) for introduction of an additional 4 vial multipack presentation and an additional 10 vial multipack presentation, respectively, to the originally approved single vial carton.

On 3 October 2002 the European Commission issued a Decision on the Type II variation procedure EMEA/H/C/369/II/08. This variation relates to updates of section 4.4, 4.8, 5.1 and 5.2 of the Summary of Product Characteristics (SPC) as a result of completion of the TKT014 study in female patients.

On 21 October 2002 the European Commission issued a Decision on a Type II variation (EMEA/H/C/369/II/11) to update part II of the dossier.

On 28 January 2003 the European Commission issued a Decision on the 1st Annual Re-Assessment (EMEA/H/C/369/S/12) of the specific obligations and the benefit/risk ratio. The marketing authorisation for Replagal remained under exceptional circumstances.

On 19 December 2002 the EMEA, following submission of a Type I variation (EMEA/H/C/369/I/13) notified a change in the name of the manufacturer of the active substance from Cambrex Bio Science Inc. to Cambrex Bio Science Baltimore Inc.

On 23 January 2003 the EMEA, further to the submission of a Type I variation, (EMEA/H/C/369/I/14) notified a minor change of manufacturing process within the scope of item 12 to Commission Regulation (EC) No 542/95, as amended.

On 17 February 2003 the European Commission issued a Decision on the Type I variation EMEA/H/C/369/I/15, regarding an extension of shelf-life as foreseen at time of authorisation.

On 19 March 2003 the EMEA, further to submission of a Type I variation (which followed a Type II procedure: EMEA/H/C/369/I/16), notified a change in the manufacturing process for the finished product. This variation falls within the scope of item No 16 of Annex I to Commission Regulation (EC) No 542/95, as amended.

On 22 July 2003 the European Commission issued a Decision on a Type II variation (EMEA/H/C/369/II/17) relating to the introduction of a new manufacturing facility for the active substance and to implement several process improvements.

On 3 October 2003 the European Commission issued a Decision on a Type II variation (EMEA/H/C/369/II/18) regarding amendments to sections 4.4 and 4.8 of the SPC, and to include changes resulting from recoding of the clinical trials safety database from the WHOART 98.3 dictionary to MedDRA 5.1.