Steps taken after granting the Marketing Authorisation

For procedures finalised after 1 November 2002 please refer to module 8B.

- The MAH submitted an application for a Type I variation in accordance with Commission Regulation (EC) No. 542/95 to extend the shelf-life of the finished product from 24 months to 36 months. A notification was issued by the EMEA and the amendment to Annex I (Summary of Product Characteristics) of the Community Marketing Authorisation was adopted on 25 September 1997.

- The MAH submitted an application for a Type I variation in accordance with Commission Regulation (EC) No. 542/95 to modify the name of the medicinal product from Tritanrix HB to Tritanrix Hep B. A notification was issued by the EMEA and the amendments to Annexes I and III (Summary of Product Characteristics, labelling and Package Leaflet) of the Community Marketing Authorisation were adopted on 30 October 1997.

- The MAH submitted an application for a Type I variation in accordance with Commission Regulation (EC) No. 542/95 to include the new Manufacturing Authorisation Holder, SmithKline Beecham Biologicals Manufacturing S.A, located in Wavre Belgium, which performs labelling and packaging of the medicinal product. A notification was issued by the EMEA on 31 October 1997 and no amendments to the Annexes of the Community Marketing Authorisation were required.

- The MAH submitted a notification in accordance with article 10(3) of Council Directive No. 92/27/EEC of 31 March 1992, to introduce changes to aspects of the Package Leaflet not connected to the Summary of Product Characteristics. A notification was issued by the EMEA and the amendment to Annex IIIB (Package Leaflet) of the Community Marketing Authorisation was adopted on 9 October 1998.

- The MAH submitted an application for a Type II variation in accordance with Commission Regulation (EC) No. 542/95 for the extension of the storage time of the DTwP bulk concentrate to 36 months, at 2-8 ºC. The EMEA adopted a positive opinion on 23 June 1999 and no amendments to the Annexes of the Community Marketing Authorisation were required.

- The MAH submitted an application for a Type I variation in accordance with Commission Regulation (EC) No. 542/95 for the scale up of the hepatitis B component of Tritanrix Hep B. The EMEA adopted a positive opinion on 29 July 1999 and no amendments to the Annexes of the Community Marketing Authorisation were required.

- The MAH submitted an application for a Type I variation in accordance with Commission Regulation (EC) No. 542/95 for the implementation of a new working seed for the hepatitis B component of Tritanrix Hep B. The EMEA adopted a positive opinion on 29 July 1999 and no amendments to the Annexes of the Community Marketing Authorisation were required.

- The MAH submitted an application for a Type I variation in accordance with Commission Regulation (EC) No. 542/95 for the introduction of a simplified method for the determination of Tetanus and Diphteria potencies. The EMEA adopted a positive opinion on 16 March 2000 and no amendments to the Annexes of the Community Marketing Authorisation were required.

- The MAH submitted an application for a Type II variation in accordance with Commission Regulation (EC) No. 542/95 to add the wording regarding sensitization to thiomersal in medicinal products as agreed by CPMP in July 1999 in section 4.4 of SPC. The EMEA adopted a positive opinion on 19 October 2000 and the amendments to Annexes I and IIIB (Summary of Product Characteristics and Package Leaflet) of the Community Marketing Authorisation were adopted on 13 March 2001.

- The MAH submitted an application for a Type II variation in accordance with Commission Regulation (EC) No. 542/95 for the approval of an additional 2-dose vial presentation. The EMEA adopted a positive opinion on 25 January 2001 and the amendments to Annexes I and IIIB (Summary of Product Characteristics and Package Leaflet) of the Community Marketing Authorisation were adopted on 3 May 2001.

- The MAH submitted an application for a Type II variation in accordance with Commission Regulation (EC) No. 542/95 for the introduction relates to a change to a Hepatitis B test procedure that affects both the Hepatitis B bulk and the DTPw HepB finished product. The EMEA adopted a positive opinion on 25 January 2001 and no amendments to the Annexes of the Community Marketing Authorisation were required.

- The MAH submitted a notification in accordance with article 10(3) of Council Directive 92/27/EEC of 31 March 1992, to introduce changes to aspects of the Package Leaflet not connected to the Summary of Product Characteristics. A notification was issued by the EMEA and the amendment to Annex IIIB (Package Leaflet) of the Community Marketing Authorisation was adopted on 17 May 2001.

- The MAH submitted an application for a Type II variation in accordance with Commission Regulation (EC) No. 542/95 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). The EMEA adopted a positive opinion on 23 August 2001 and no amendments to the Annexes of the Community Marketing Authorisation were required.

Subsequent post Marketing Authorisation applications agreed upon are summarised in the table below:

Scope	Application number	Type of modification[1]	Notification/ Opinion issued on[2]	Commission Decision Issued/amended on
5-year Renewal	R/014	R	30.03.01	21.11.01
Quality change	II/015	II	20.09.01	08.10.01
Change in or addition of manufacturing site(s) for part or all of the manufacturing process	I/016	I	22.08.01	07.09.01
Change in the name of manufacturing site	I/017	I	16.11.01	
Change in the name of MAH and manufacturer responsible for batch release	I/018	I	05.11.01	29.01.02
Quality change: Quality: Change(s) to the manufacturing process for the active substance Quality: Change(s) to the manufacturing process for the finished product	II/019	II	19/09/02	25.09.02
Minor changes to the Patient Leaflet regarding some MAH local representative details	N/025	N	19/09/02	10/10/02

[1] In accordance with Commission Regulation (EC) No. 542/95 of 10 March 1995, as amended: **I** refers to a minor variation (Type I variation); **II** refers to a major variation (Type II variation); **I/II** refers to a minor variation following the procedure set out in Article 6, 7 and 8 of the Regulation; **X** refers to an Annex II application.
T refers to a transfer of a Marketing Authorisation in accordance with Commission Regulation (EC) No 2141/96 of 7 November 1996.
N refers to a notification in accordance with Article 10(3) of Council Directive 92/27/EEC of 31 March 1992.

[2] For Notifications and Type I variations, the date of entry into force of the change is the EMEA Notification date. The Commission Decision will be amended accordingly.