STEPS TAKEN AFTER GRANTING THE MARKETING AUTHORISATION

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

On 30 April 1996 the European Commission issued a marketing authorisation valid throughout the European Union for the medicinal product Humalog. This decision was based on the assessment report and on the favourable opinion adopted by the Committee for Proprietary Medicinal Products (CPMP) on 22 November 1995 for Humalog. Table N°1 summarise subsequent post Marketing Authorisation applications for Humalog issued by Commission Decision until 18 April 2001.

The company Eli Lilly B.V. Nederland submitted to the EMEA an application to extend the marketing authorisation, concerning Humalog (100 U/ml) 3.0 ml cartridge and Humalog-HumaJect (100U/ml) 3.0 ml cartridge in a disposable pen. The CPMP issued on 20 November 1996 a positive opinion for granting the marketing authorisation to Humalog 3.0 ml cartridge and to Humalog-HumaJect 3.0 ml cartridge in a disposable pen. Table N°2 summarise subsequent post Marketing Authorisation applications for Humalog-HumaJect issued by Commission Decision until 18 April 2001.

Eli Lilly B.V. Nederland submitted to the EMEA an application to extend the marketing authorisation for Humalog-HumaPen (100U/ml) 3.0 ml cartridge in a disposable pen. The CPMP issued a positive opinion for granting the marketing authorisation on 18 February 1997. Table N°3 summarise subsequent post Marketing Authorisation applications for Humalog-HumaPen issued by Commission Decision until 18 April 2001.

During the variation EMEA/H/C/0088/II/23 for Humalog the MAH requested to combine all 17 insulin lispro presentations of the Humalog, Humalog-HumaJect and Humalog Pen licences into the one core Humalog licence (EU/1/96/007). Table N°4 summarise subsequent post Marketing Authorisation applications for all Humalog, Humalog-HumaJect and Humalog Pen licences.

TABLE N°1 APPLICATIONS FOR HUMALOG ISSUED BY COMMISSION DECISION UNTIL 18 APRIL 2001.

Scope	Application number	Type of modification[1]	Notification/ Opinion issued on[2]	Commission Decision Issued/amended on
Change in the name of a manufacturer of the medicinal product	I/II/001	I	16.06.96	26.08.96
Change in the name of a manufacturer of the medicinal product	I/II/002	I	02.10.96	05.12.96
Change in the content of the manufacturing authorization	I/II/003	I	13.05.97	29.07.97
Minor change of manufacturing process of the active substance	I/II/004	I/II	13.05.97	29.07.97
Inclusion of an additional reusable insulin pen (Autopen) for 1.5 ml cartridges	II/005	II	13.05.97	16.06.97
Update of summary of product characteristics concerning use in children and possibility of postprandial administration	II/006	II	23.07.97	01.12.97
Replacement of the names of specific insulin injector pens with "compatible CE marked pen" statement.	II/0007	II	24.09.97	10.03.98
Increase of manufacturer batch size for Humalog 1.5 ml cartridges	I/008	I	24.09.97	
New safety warning	II/009	II	23.07.97	01.12.97
Addition of a new route of administration and new safety warning	II/010	II	17.12.97	11.05.98
Extension and abridged applications	X/011	X	23.07.98	19.11.98 CD for 1 withdrawal Pres. 30.07.99

[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 or consequently with Article 61(3) of Council Directive 2001/83/EC

[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.

Change in the name of the medicinal product	I/012(01)	I	30.10.98	26.01.99
Change in the name of the medicinal product	I/013	I	30.10.98	
Change in the name of a manufacturer of the medicinal product	I/014	I	23.02.99	03.06.99
Update of summary of product characteristics, labelling and package leaflet, regarding renal and hepatic impairment	II/015	II	20.05.99	10.11.99
Change in Manufacturing site	II/016	II	24.06.99	
Additional stopper	II/017	II	29.07.99	
Minor change of manufacturing process of the active substance	I/II/018	I/II	29.07.99	
Minor change of manufacturing process of the active substance	I/II/019	I/II	29.07.99	
Update of summary of product characteristics and package leaflet regarding the use of Humalog in children	II/020	II	16.12.99	13.04.00
Change in batch size of finished product	I/II/0021	I/II	28.08.00	12.10.00
Change in batch size of finished product	I/II/0022	I/II	28.08.00	12.10.00
Update of summary product characteristics with regard to safe use in children	II/0023	II	25.01.01	18.05.01

TABLE N°2 APPLICATIONS FOR HUMALOG-HUMAJECT ISSUED BY COMMISSION DECISION UNTIL 18 APRIL 2001.

Scope	Application number	Type of modification[1]	Notification/ Opinion issued on[2]	Commission Decision Issued/amended on
Update of summary of product characteristics concerning use in children below 12 years of age and possibility of postprandial administration	II/0001	II	23.07.97	01.12.97
Change in or addition of manufacturer of active substance	I/II/002	I/II	23.07.97	
Minor change of manufacturing process of the active substance	I/II/003	I/II	23.07.97	
New safety warning	II/0004	II	23.07.97	28.11.97 01.12.97
Addition of a new route of administration and new safety warning	II/0005	II	17.12.97	15.04.98
Extension and abridged applications	X/0006	X	23.07.98	19.11.98
Extension and abridged applications	X/0007	X	23.07.98	19.11.98
Change in batch size of finished product	I/0008	I	22.04.98	
Minor change in labelling or package leaflet not connected with the SPC (Art. 10.3 Notification)	N/0009	N	06.08.98	21.10.98
Change in the name of the medicinal product (either invented name of common name)	I/0010	I	30.10.98	26.01.99
Change in the name of the medicinal product (either invented name of common name)	I/0011	I	30.10.98	27.01.99
Update of summary of product characteristics, labelling and package leaflet regarding renal and hepatic impairment	II/0012	II	20.05.99	10.11.99
Minor change of manufacturing process of the active substance	I/II/0014	I/II	29.07.99	04.08.99
Minor change of manufacturing process of the active substance	I/II/0015	I/II	20.07.99	04.08.99
Update of summary of product characteristics and package leaflet regarding the use of Humalog in children	II/0016	II	16.12.99	30.03.00
Change in the batch size of finished product	I/II/0017	I/II	28.08.00	
Change in the batch size of finished product	I/II/0018	I/II	28.08.00	

[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 or consequently with Article 61(3) of Council Directive 2001/83/EC

[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.

TABLE N°3 APPLICATIONS FOR HUMALOG-HUMAPEN ISSUED BY COMMISSION DECISION UNTIL 18 APRIL 2001.

Scope	Application number	Type of modification[1]	Notification/ Opinion issued on[2]	Commission Decision Issued/amended on
Change in or addition of manufacturer of active substance	I/II/001	I	23.06.97	
Minor change of manufacturing process of the active substance	I/II/002	I	23.06.97	
Change in the name of the medicinal product (either invented name or common name)	I/003	I	04.08.97	27.10.97
New safety warning	II/005	II	22.10.97	03.03.98
Addition of a new route of administration and new safety warning	II/006	II	17.12.97	14.04.98
Extensions and abridged applications	X/007	X	23.07.98	19.11.98
Change in the batch size of finished product	I//008	I	22.04.98	
Minor change in labelling or package leaflet not connected with the SPC (Art. 10.3 Notification)	N/009	N	30.04.98	
Change in the name of the medicinal product (either invented name or common name)	I/010	I	30.10.98	26.01.99
Update of summary of product characteristics, labelling and package leaflet, regarding renal and hepatic impairment	II/011	II	20.05.99	30.09.99
Minor change of manufacturing process of the active substance	I/II/013	I/II	29.07.99	04.08.99
Minor change of manufacturing process of the active substance	I/II/014	I/II	29.07.99	04.08.99
Update of summary of product characteristics and package leaflet regarding the use of Humalog in children	II/015	I	16.12.99	30.03.00
Changes in manufacture of the medicinal product	I/016	I	15.03.00	
Change in the batch size of finished product	I/017	I	28.08.00	
Change in the batch size of finished product	I/018	I	28.08.00	

TABLE N°4 APPLICATIONS FOR ALL HUMALOG, HUMALOG-HUMAJECT AND HUMALOG PEN LICENCES AFTER 18 APRIL 2001.

Scope	Application number	Type of modification[1]	Notification/ Opinion issued on[2]	Commission Decision Issued/amended on
5 years Renewal	R/024	R	01.03.01	27.06.01
Quality changes, demonstration of TSE compliance	II/025	II	28.06.01	04.07.01
Change in the name and/or address of the marketing authorisation holder	I/026	I	22.02.01	
Quality changes, demonstration of TSE compliance	II/027	II	28.06.01	04.07.01
Quality changes concerning new manufacturing building	II/028	II	26.04.01	03.05.01
Additional route of administration (intravenous)	X/029	X	15.11.01	21.03.02
Update of Summary of Product Characteristics and Package Leaflet regarding the use of Humalog with sulphonylurea drugs	II/030	II	26.07.01	09.11.01
Update of Summary of Product Characteristics regarding data on the reduction of postprandial hyperglycaemia	II/031	II	26.07.01	09.11.01
Update of Summary of Product Characteristics regarding data on reduction of nocturnal hypoglycaemia	II/032	II	26.07.01	09.11.01
Update of Summary of Product Characteristics and Package Leaflet regarding data from animal studies and with current information concerning pregnancy	II/033	II	26.07.01	09.11.01
Additional new presentation (vial) of the Humalog Mix50 formulation	II0034	II	26.07.01	09.11.01
Changes in manufacture of the medicinal product	I/035	I	25.04.02	
Minor change in labelling or package leaflet not connected with the SPC	N/036	N	14.05.02	17.06.02
Change in pack size of the medicinal product	I/037	I	30.07.02	

[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 or consequently with Article 61(3) of Council Directive 2001/83/EC.

[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.

Change in or addition of manufacturing site(s) for part or all of the manufacturing process	I/038	I	19.09.02	13.11.02
Minor change in labelling or package leaflet not connected with the SPC	N/039	N	19.09.02	13.11.02
Change in pack size of the medicinal product	I/040	I	13.11.02	16.12.02
Change in specification of the medicinal product	I/041	I	04.03.2003	
Update of incompatibilities and instruction for use section of Summary of Product Characteristics and Package Leaflet	II/042	II	22.05.2003	07.08.2003
Minor change of manufacturing process of the active substance	I/043	I	24.07.2003	
Change in the batch size of finished product	I/044	I	24.07.2003	
Update of Pregnancy data of Summary of Product Characteristics	II/045	II	24.07.2003	11.11.2003
Minor changes to the finished product filing line (CGV1) which is used for the production of 3.0 ml cartridges for several authorised presentations	I/046	I	20.11.2003	
Minor change in package leaflet and user manual not connected with the SPC	N/047	N	17.11.2003	
Minor change in the manufacturing process of the active substance	II/048	II	24.03.2004	
Use of an additional manufacturing facility for the formulation and filling of Humalog 3.0 ml cartridges, 100 IU/ml.	II/049	II	03.06.2004	
Minor change in package leaflet not connected with the SPC	N/050	N	12.05.2004	
Change in the name of a manufacturer of the finished product	IA/ 051	IA	22.06.2004	