BACKGROUND INFORMATION ON THE PROCEDURE

1. Submission of the dossier

The company Eli Lilly Industries Nederland B.V. submitted an application to all EU Member States for Humalog, through the Concertation procedure No 88 on 1 November 1994.

In application to Article 2 of Directive 93/41/EEC on January 1995 the company Lilly Industries Limited transferred to the European Agency for the Evaluation of Medicinal Products, into the new centralised procedure, the application for marketing authorisation for Humalog falling within the scope of Part B of the Annex to Council Regulation (EEC) No. 2309/93 of 22 July 1993.

The CPMP confirmed the status of Rapporteur as follows:

Rapporteur: Dr D.Jefferys

Licensing status:

Humalog has been given a marketing authorisation in the following countries:

Argentina	February 1997	New Zealand	November 1996
Australia	May 1996	Norway	September 1996
Brazil	June 1996	Poland	December 1996
Bulgaria	December 1996	Philippines	December 1996
Canada	October 1996	Romania	August 1996
Czech. Rep.	February 1996	Russia	April 1995
Hungary	February 1997	Slovakia	October 1996
Iceland	October 1996	South Africa	September 1995
Israel	September 1996	Switzerland	November 1995
Latvia	Approved	Ukraine	Approved
Lithuania	Approved	USA	June 1996

2. Steps taken for the assessment of the product

- The Rapporteur's initial assessment report was circulated to all Members of the CPMP on 18 January 1995.
- The CPMP during their meeting on March 1995 agreed that the application should be considered at the Biotechnology Working Party meeting on 6-7 April 1995.
- The Rapporteur drew up a draft of the consolidated list of questions related to quality on 5 April 1995 for consideration at the Biotechnology Working Party meeting on 6-7 April 1995.
- A consolidated list of questions for Pre-clinical (Part III) and Clinical (Part IV and SmPC) was circulated on 18 April 1995 by the Rapporteur and was endorsed by the CPMP meeting on 26-27 April 1995, and sent to the company on 22 May 1995.
- A second consolidated list of questions was sent to the company on 26 June 1995 as agreed at the CPMP meeting that took place on 7-8 June 1995. As 40 U and 100 U strengths of insulin are available in different Member States, the EMEA Secretariat requested the company to comment on implementing measures to prevent potential unsafe use of different strengths of Insulin lispro.
- The company submitted the responses to the consolidated CPMP list of questions on 3 August 1995.
- The Rapporteurs' Assessment Report on the company's responses was sent out to all members of the CPMP on 22 September 1995.
- The Rapporteur circulated to all CPMP Members the assessment report on the proposal for a new Summary Product of Characteristics on 11 October 1995.
- Company responses to the Rapporteur's Assessment Report were provided on 12 October 1995.

- The Rapporteur circulated an additional assessment report on the outstanding pharmaceutical responses provided by the company on 13 October 1995.
- The CPMP during the meeting held on 17-19 October 1995, discussed the recommendations presented by the Rapporteur and the responses provided by the Company. The following points were considered: a) the legal status (subject to renewable medical prescription) and the potential implications of public health on marketing 40 U/ml and 100U/ml vials; b) the specific obligations of the marketing authorisation holder on providing additional information on the pharmaceutical dossier; c) a revised section 4.5 (interactions) on the Summary of Product Characteristics; d) the Company was requested to provide additional 'in-vitro cell studies' before the November CPMP Meeting.
- The Company submitted to all CPMP Members the results of the 'in-vitro cell studies' on 6 and 16 November 1995.
- The Biotechnology Working Party meeting held on 13-14 November agreed on granting a positive opinion provided that the company within the agreed timeframe as described in section II.3 of this assessment report submits additional information on the pharmaceutical dossier.
- The CPMP members, during the meeting held on 20-21-22 November 1995, discussed the possibility of confusion created by the presence of different strengths. The company will ensure that there is clear differentiation on the outer packaging of the different strengths.
- The CPMP in the light of current scientific standards issued on 22 November 1995 three positive opinions for granting a marketing authorisation to different presentations of Humalog (10 ml vials of 40 U/ml and 100 U/ml, 1.5 ml cartridge of 100 U/ml).