BACKGROUND INFORMATION ON THE PROCEDURE

1. Submission of the dossier

The company Roche Registration Limited submitted on 11 February 1999 an application for Marketing Authorisation to the European Agency for the Evaluation of Medicinal Products (EMEA) for Herceptin in accordance with the centralised procedure falling within the scope of Part A of the Annex to Council Regulation No (EEC) 2309/93 of 22 July 1993.

The Rapporteur and Co-Rapporteur appointed by the CPMP were:
Rapporteur: Dr. M. Haase Co-Rapporteur: Dr. F. Rotblat

Licensing status:
The product was licensed in the U.S. at the time of submission of the application.

2. Steps taken for the assessment of the product

- The procedure started on 26 February 1999
- The Rapporteur's first assessment report was circulated to all CPMP Members on 12 May 1999 (Annex 1). The Co-Rapporteur's first assessment report was circulated to all CPMP Members on 17 May 1999 (Annex 2)
- During the meeting on 16 June 1999 the BWP agreed on the list of questions on Part II and adopted a recommendation to the CPMP. (Annex 3).
- During the meeting on 22 June 1999 the CPMP agreed on the consolidated list of questions to be sent to the company. The final consolidated list of questions was sent to the company on 23 June 1999 (Annex 4).
- At a meeting with the Rapporteur and Co-Rapporteur teams, the EMEA and the applicant on 28 July 1999, issues from the List of Questions on Part II and Part IV were discussed in preparation of the Applicant's response.
- The company submitted the responses to the CPMP consolidated list of questions on 30 November, 1999. This submission was incomplete in that it did not contain data on production scale of the finished product batches at the intended site of manufacturing. In view of the potential importance of the product to the public health, the Rapporteur / Co-Rapporteur in agreement with the CPMP prepared a joint assessment report on these incomplete responses
- This joint assessment report was circulated on 3 February 2000 (Annex 5).
- The summary report of the inspection carried out at the manufacturing sites between 13-16 December 1999 of the Genentech Vacaville, USA was issued on 10 February 2000 (Annex 6)
- On 6 March 2000 the Rapporteur/Co-Rapporteur teams met to discuss the outstanding questions on Part II. The outcome of this discussion was reported to the BWP on 7 March 2000.
- During the meeting on 7 March 2000 1999 the BWP adopted a recommendation to the CPMP on outstanding quality points. (Annex 7).
- During the meeting on 14-17 March 2000 the CPMP agreed on the consolidated list of outstanding issues to be addressed by the company in writing and at an oral explanation. (Annex 8)
- The Rapporteur and Co-Rapporteur teams met with the applicant on 14 March 2000 and discussed the outstanding points from the consolidated CPMP list of questions.
- The company submitted the responses to the CPMP consolidated list of questions with regard to outstanding quality issues on 24 March 2000

- The summary report of the inspection carried out at the manufacturing sites between 28 February and 1 March 2000 1999 of the manufacturing site at Roche Basel, Switzerland was issued on 6 April 2000 (Annex 9)
- Supplementary information related to safety was requested from the applicant on 30 March 2000 and the procedural clock was stopped on 30 March 2000.
- The joint Rapporteur / Co-Rapporteur Assessment Report assessment report on the company's responses to the quality points was sent to all CPMP Members on 3 April 2000 (Annex 10)
- The applicant submitted supplementary information to the clinical part and the 2nd PSUR on 17 April 2000
- The joint Rapporteur / Co-Rapporteur Assessment Report on the outstanding pre-clinical and clinical points and on the 2nd PSUR was circulated to all CPMP Members on 3 May 2000 (Annex 11)
- During the CPMP meeting on 24 May 2000, outstanding clinical issues were addressed by the applicant during a hearing before the CPMP.
- During the meeting on 23-25 May 2000 the CPMP, in the light of the overall data submitted and the scientific discussion within the Committee, issued a positive opinion by majority vote for granting a Marketing Authorisation to Herceptin on 25 May 2000.
  The indication:

  "Herceptin is indicated for the treatment of patients with metastatic breast cancer whose tumours overexpress HER2: in combination with paclitaxel for the treatment of those patients who have not received chemotherapy for their metastatic disease and for whom an anthracycline is not suitable."

  Was accepted by a majority of 26 out of 26 votes and 1 abstention.
  The indication:

  "Herceptin is indicated for the treatment of patients with metastatic breast cancer whose tumours overexpress HER2: as monotherapy for the treatment of those patients who have received at least two chemotherapy regimens for their metastatic disease. Prior chemotherapy must have included at least an anthracycline and a taxane unless patients are unsuitable for these treatments. Hormone receptor positive patients must also have failed hormonal therapy, unless patients are unsuitable for these treatments."

  Was accepted by a majority of 20 out of 26 votes and 1 abstention.
- The applicant committed to submit the Follow Up Measures within the defined timeframe by letter of undertaking, dated 24 May 2000. (Annex 12)