BACKGROUND INFORMATION ON THE PROCEDURE

1. Submission of the dossier

The company Roche Registration Limited submitted on 15 September 1995 an application for Marketing Authorisation to the European Agency for the Evaluation of Medicinal Products (EMEA) for Invirase (saquinavir) 200 mg hard capsules through the centralised procedure. After agreement by the CPMP on 11 July 1995, this medicinal product is referred to Part B of the Annex of the Council Regulation (EEC) No 2309/93 of the 22 July 1993; indent 7 as it contains a new active substance.

The Rapporteur and the Co-Rapporteur appointed by the CPMP were:

Rapporteur: Dr. H. Pittner Co-Rapporteur: Prof. K. Strandberg

Licensing status:

Invirase has been approved in several countries including the USA, Switzerland, Canada and Australia.

2. Steps taken for the assessment of the product

- An application for marketing authorisation for Invirase was submitted to the EMEA on 15 September 1995. The centralised procedure started on 2 October 1995.
- During the December CPMP Meeting 1995, it was agreed to perform a GMP inspection on the Switzerland manufacturing facility for the finished medicinal product by the German inspectorates. The inspection took place on 12-14 February 1996.
- The Co-Rapporteur's assessment report was circulated to all CPMP Members on 15 December 1995. The Rapporteur's assessment report was circulated to all CPMP Members on 18 December 1995.
- A breakout session between Rapporteur and Co-Rapporteur evaluation teams was held on 2 February 1996 to prepare a draft consolidated list of questions.
- The consolidated list of questions as agreed by the CPMP on 14 February 1996, was sent to the applicant.
- The joint Rapporteur and Co-Rapporteur assessment report on the responses on the consolidated list of questions was circulated to all CPMP Members on 28 May 1996.
- An extended assessment report of the clinical study NV14256 was circulated to all CPMP Members by the Co-Rapporteur on 31 May 1996 and the Rapporteur on 3 June 1996.
- A hearing with the applicant was held on 18 June 1996 during the June CPMP meeting to address the strategy of ongoing clinical studies with particular emphasis on those studies, which are intended to new pharmaceutical forms and new dosage regimens.
- The applicant submitted on 19 June 1996 their letter of commitments for providing information on clinical aspects (submission of final reports of the ongoing clinical studies NV14256 and 14604) as part of the re-assessment of the benefit/risk profile. The applicant also committed it to provide additional data regarding quality, safety and efficacy aspects.
- The CPMP in the light of the overall data submitted and the scientific discussion within the Committee issued on 20 June 1996 a positive opinion for granting a Marketing Authorisation for Invirase under exceptional circumstances.
- Following a rapid alert from France on the 14 June 1996 drawing attention to reports of spontaneous bleedings in haemophiliac patients involved in the "Autorisation Temporaire d'Utilisation (ATU)" programme, the CPMP during their meeting of 16-17 July 1996 agreed to revise the opinions adopted on 19 June 1996. In the revised opinions, warnings have been

introduced into the Summary of Product Characteristics and in the Package Leaflet in the light of the information available.

- The wordings proposed by the CPMP were discussed between the Chairman of the Committee and the companies involved in the marketing of protease inhibitors. An agreement on the warnings to be introduced was reached on Monday 22 July 1996.
- The CPMP revised opinion was forwarded, in all official languages of the European Union, to the European Commission, which adopted the corresponding Decision on 4 October 1996.