LÄKEMEDELSVERKET
MEDICAL PRODUCTS AGENCY

MUTUAL RECOGNITION VARIATION RESPONSE REPORT

1 COMMENTS FROM THE MEDICAL PRODUCTS AGENCY ON THE FINAL VARIATION ASSESSMENT REPORTS (FVARS)

Name:	**Prozac (Fontex, Fontex Basal)**
Procedure No.:	UK/H/636/1,3/II/02 :
Dosage form and strength:	**20 mg capsules; 20 mg/5ml oral liquid**
Date of the Response Report:	April 29, 2005

Name:	**Prozac (Fontex, Fontex Basal)**
Procedure No.:	FR/H/242/01/II/002
Dosage form and strength:	**20 mg dispersible tablet**
Date of the Response Report:	April 29, 2005

On 11 March 05, the MPA raised 'potentially serious public health concerns' within the FR procedure (FR/H/242/01/II/002) for a pediatric indication for fluoxetine, by supporting issues raised by FR as well as pointing to additional questions to be solved before recommendation of approval (Appendix 1). Although concerns remain regarding these points (see further below), the MPA currently supports the overall view of the UK, i.e. that approval may be recommended provided commitments of further studies and appropriate wording of the SPC. It is a fact that SSRIs, including fluoxetine, are used 'off label' in children and adolescents, and approving use of fluoxetine allows for providing treatment recommendations, better post marketing surveillance in these populations and possibilities to request further studies. In addition, in 2002, the CPMP issued a positive opinion within a referral (EMEA/H/A/-11/376) for another SSRI, **fluvoxamine,** which resulted in dose recommendations for the treatment of OCD in patients aged 8-17 years. Similar safety concerns were discussed at that time. Nevertheless, we also find it important that the timing of approval is considered, and would be in favour of awaiting the finalisation (i.e. Commission Decision) of the ongoing referral for SSRIs.

COMMITMENTS OF FUTURE STUDIES:

We agree with the UK proposal. In addition, we support the comment by FR (AR dated 5 April 2005), that further work should be undertaken to explore the mechanisms of the testicular toxicity observed in the juvenile toxicity study.

RESTRICTION OF PATIENT POPULATION:

Until additional data become available, we suggest that only patient having reached/passed puberty are to be treated with fluoxetine, since main safety concerns are related to potential effects on growth and sexual development. Appropriate wording of the SPC should be included.

DOSE RECOMMENDATION

During the break-out session, the UK stated that the maximum recommended dose has been changed to 20 mg/d, which should be confirmed. Moreover, one issue raised by SE in Mar 04 has not been adequately addressed by the MAH, and should be responded to, namely: