**Appendix 1**

## Conditions and Principles which apply to the Inclusion of an Incapacitated Adult in a Clinical Trial

### Conditions

1. The legal representative has had an interview with the investigator, or another member of the investigating team, in which opportunity has been given to understand the objectives, risks and inconveniences of the study and the conditions under which it is to be conducted.

2. The legal representative has been provided with a contact point where further information about the study may be obtained.

3. The legal representative has been informed of the right to withdraw the subject from the study at any time.

4. The legal representative has given informed consent to the subject taking part in the study.

5. The legal representative may, without the subject being subject to any resulting detriment, withdraw the subject from the study at any time by revoking the informed consent.

[Note: Paragraphs 1-5 do not apply where treatment is being, or is about to be, provided for a subject who is an incapacitated adult as a matter of urgency and, having regard to the nature of the clinical study and of the particular circumstances of the case:

- It is also necessary to take action for the purposes of the study as a matter of urgency; but
- It is not reasonably practicable to meet the conditions set out in paragraph 1-5; and
- The action taken is carried out in accordance with a procedure approved by the ethics committee.]

6. The subject has received information, according to his or her capacity of understanding, about the study and its risks and benefits.

7. The investigator must consider the explicit wish of a subject capable of forming an opinion and assessing the information provided. This applies both to the wish of a subject to refuse to take part, or to withdraw from the study at any time.

8. No incentives or financial inducements are given either to the subject or to the legal representative, except the provision of compensation for injury or loss.

9. There are grounds for expecting that administering the medicinal product to be tested in the study will produce a benefit.

10. The study is essential to validate data obtained (a) in other clinical trials involving persons able to give informed consent, or (b) by other research methods.

11. The clinical study relates directly to a life-threatening or debilitating clinical condition from which the subject suffers.

**Principles**

12. Informed consent given by a legal representative shall represent the presumed will of an incapacitated adult.

13. The study has been designed to minimise pain, discomfort, fear and any other foreseeable risk in relation to the disease and the cognitive abilities of the patient.

14. The risk threshold and the degree of distress have to be specially defined and constantly monitored.

15. The interests of the patient always prevail over those of science and society.