INFORMED CONSENT

InfCons-Typ = Type of informed consent
InfCons-Conf = Confirmation of consent
InfCons-DatTim = Date and time written consent signed

<table>
<tr><td>1. CDE Variable</td><td colspan="2">InfCons-Typ = Type of initial consent
InfCons-Conf = Confirmation of consent
InfCons-DatTim = Date and time written consent signed</td></tr>
<tr><td>2. CDE Definition</td><td colspan="2">Type of initial consent designates the approach taken for obtaining permission to enrol the patient into the study. The confirmation of consent documents how written consent for (continued) participation was obtained.</td></tr>
<tr><td>3. Recommended instrument for assessment</td><td colspan="2">N/A.</td></tr>
<tr><td>4. Description of measure</td><td colspan="2">Date, time: hours/minutes.
Type and confirmation of consent: categorical; unique entry.</td></tr>
<tr><td rowspan="2">5. Permissible values</td><td><u>Type of initial consent</u>
Basic/intermediate:
- informed consent (by subject)
- proxy consent
- consent by independent physician
- deferred consent
- waiver of consent (including EFIC*)

* EFIC = Exception from informed consent</td><td>
advanced:
- informed consent (by subject)
- oral
- written
- proxy consent
- by telephone
- written
- consent by independent physician
- by telephone
- written
- deferred consent
- waiver of consent
- Exception from informed consent (EFIC, US only)</td></tr>
<tr><td colspan="2"><u>Confirmation of consent</u>
(Basic/intermediate/advanced)
- written proxy consent before enrolment
- written proxy consent after enrolment
- written informed consent by patient

<u>Date and time of initial consent:</u>
Date/time written consent signed
Date: DD-MMM-YYYY
99-999-9999 if unknown
Time: HH-MM (24 hour clock)
99-99 if unknown</td></tr>
<tr><td>6. Classification: Basic/Intermediate/Advanced</td><td colspan="2">Identical</td></tr>
<tr><td>7. Procedure</td><td colspan="2">Document the type of initial consent for enrolment of the</td></tr>
</table>

	patient into the study and in the intermediate version also the date and time that this was obtained; this must be prior to any study related intervention. When required by national legislation or local IRB, please additionally document how written confirmation of consent was obtained and the date and time thereof (advanced version).

8. Comments / Special instructions:

Accepted approaches to informed consent procedures in acutely mentally incapacitated patients such as in TBI and then frequently in an emergency situation vary considerably between and even within countries. Approaches taken must comply with national regulations and be accepted by the local IRB. We recognize the following main types of informed consent procedures:

Informed consent: consent given on basis of verbal or written information, either by patient of legal representative.

Proxy consent: consent given by someone else than the patient, e.g. a legal representative or relative of the patient.

Consent by an independent physician: consent by a physician not directly related to the researcher or the department of the researcher, with no conflict of interest by the research project.

Deferred consent: consent given after enrolment by patient (deferred patient consent) or proxy (deferred proxy consent).

Waiver of consent: partially waived consent, or waiver or alteration of all elements of consent (e.g. no verbal and no written consent).

EFIC (Exception from Informed Consent) was introduced in the U.S. to allow emergency research in settings of a life threatening disorder, and is currently widely employed. As a special form of "waiver of consent", EFIC is subject to very strict rules and regulations, written in the Federal Register 21 CFR 50.24. These rules include that it must be reviewed by the FDA, and requires both community consultation and adequate public disclosure. Where possible, patient or proxy consent should be sought later, but is not considered mandatory (in case of death, or when no relatives can be found). In every case in which EFIC procedures are followed, concerted efforts for obtaining (deferred) consent should be documented.

9. Rationale / justification:

Accurate documentation of informed consent procedures is mandatory for all clinical studies, also those without study related interventions. Accurate documentation of informed consent procedures employed, the time of obtaining consent and where appropriate the time of subsequent written confirmation is highly relevant and can be motivated from a legal and moral perspective and is mandatory in order to comply with ethical regulations.

10. References:

Kompanje EJ, Maas AI, Hilhorst MT, et al. Ethical considerations on consent procedures for emergency research in severe and moderate traumatic brain injury. *Acta Neurochir (Wien)*. Jun 2005;147(6):633-9; discussion 639-40.

Kompanje EJ, Maas AI. 'Treat first, ask later?' Emergency research in acute neurology and neurotraumatology in the European Union. *Intensive Care Med*. Jan 2004;30(1):168-9. Epub 2003 Nov 21

Stocchetti N, Dearden M, Karimi A, et al. New European directive on clinical trials: implications for traumatic head injury research. *Intensive Care Med*. Mar 2004;30(3):517-8.

Directive 2001/20/EC of the European Parliament and of the Council of 4 April 2001 on the approximation of the laws, regulations and administrative provisions of the Member States

relating to the implementation of good clinical practice in the conduct of clinical trials on medicinal products for human use. *Official J Eur Commun* 1–5-2001, L 121/34–44

Recommended time for assessment:
Prior to enrolment to study.