## Grade of severity

* *Mild (grade 1)*: patient is aware of symptoms but tolerates them easily. Symptoms do not interfere with daily activity.
* *Moderate (grade 2)*: patient experiences discomfort that interferes with normal activity. No treatment is required except acetaminophen.
* *Severe (grade 3):* patient is unable to carry out normal activity. Treatment is required.
* *Life-threatening (grade 4)*: emergency room visit , disabling or hospitalization.

## Anticipated Adverse Events to be reported

* The following anticipated adverse events need to be reported within one week after becoming aware of the event irrespective of seriousness criteria:
  + Venous or arterial thrombosis
  + Rejection
  + Graft loss

The investigator will exercise his/her medical judgment in deciding whether a postoperative laboratory finding falling outside the relevant reference range or other abnormal assessment is clinically significant. However, if in the opinion of the investigator, the frequency or severity of the event is greater than would be expected then it must be reported.

## Protocol-defined Events

All anticipated adverse events are protocol-defined events and do not require immediate reporting.

* All other anticipated adverse events will be reported at the time of study visits (day 7, 3, 6 and 12 months after transplantation) irrespective of seriousness criteria.
* The following adverse events are very common features in kidney transplant recipients and are not considered adverse events for the purpose of the trial:
  + Gastrointestinal problems (nausea, constipation and/or diarrhoea) related to the use of immunosuppression (such as mycophenolate acid derivatives)
  + Hypertension as a pre existing disease or induced by immunosuppression
  + Headaches related to immunosuppression
  + Anaemia, Leukopenia or thrombocytopenia related to immunosuppression
  + Transient hyper/hypocalcemia, hyper/hyponatremia, hyper/hypokalaemia, hyper/hypophosphataemia, hypomagnesemia are expected during the peri-operative period after kidney transplantation
  + Transient abnormal liver function tests induced by medication given to a kidney transplant patient
  + Peripheral oedema and hypoalbuminemia in the peri-operative period related to filling status and peri-operative management (until first 3 months after kidney transplantation)

## Recording adverse events and device deficiencies

It is the responsibility of the Local Investigator to ensure that all adverse events (including ADEs) and device deficiencies occurring during the course of the study are recorded. This will include but not be limited to:

* A description of the event
* The dates of the onset and resolution
* Action taken
* Outcome
* Assessment of relatedness to the device
* Whether the AE is serious or not
* Whether the AE arises from device deficiency
* Whether the AE arises from user error

Adverse events that occur during the course of the study should be treated by established standards of care that will protect the life and health of the study subjects.

It is the responsibility of the Local Investigator to collect all directly observed adverse events and all adverse events spontaneously reported by the subject. In addition each subject should be questioned about adverse events at each visit. Adverse events should be recorded on provided adverse event data collection forms within the eCFR.

## Reporting procedures for all serious adverse events

Reporting of all Serious Adverse Events will be done in accordance with the European Commission Guidelines on Medical Devices Serious Adverse Event Reporting (MEDDEV 2.7/3; December 2010).

It is the responsibility of the local investigator to ensure that all adverse events which fall in to the category of Serious Adverse Events (SAEs) and any device deficiencies (including Serious Adverse Device Effects (SADEs)) are reported to the coordinating centre, chief investigator, principle investigator, national investigators as soon as possible after becoming aware of the event but no later than 24 hours. Details to be included in the report are as Section 10.5.

Adverse event and serious adverse event reporting will be via the electronic data collection tool using the COPE SAE form, with SAEs being automatically forwarded to the Trial Coordinator and clinical reviewers by the reporting tool. The clinical reviewers are the Chief Investigator, Principle Investigator and Central Investigator and National Investigators. Reporting by Fax will provide a backup system (+32 (0)16 34 87 43) in the event that the online data collection tool is unavailable. The Fax machine is located in the central coordinating centre and is manned during normal office hours only.

Within the following 5 working days, the Local Investigator should provide any additional information on the initial SAE or device deficiency in the form of a written narrative using the same SAE form submitted initially – do not create a new form for follow up information. This should include a copy of the completed SAE form, and any other diagnostic or relevant information that will assist the understanding of the event. Significant new information on ongoing serious adverse events should be provided promptly to the coordinating centre and clinical reviewers using the same electronic COPE SAE form.

On submission of an electronic SAE form, the co-ordinating centre and all of the clinical reviewers will be immediately notified by email. They will review SAEs and, if they feel they pose an immediate risk to patient health or safety, then they will report them to the DMC immediately and to the device manufacturer and research ethics committees within 2 calendar days of the principle Investigator becoming aware of the event.

All other reported SAEs will be reported to the DMC within 7 calendar days of notification, if appropriate. This will not include SAEs that may be expected as part of the risks of kidney transplant surgery. Adverse device events (SADEs, USADEs) and device deficiencies will also be reported to the device manufacturer. All SAEs will be followed up to resolution. The DMC will review the accumulating data at regular intervals.

The Principle Investigator will also inform all investigators concerned and the device manufacturer of relevant information about USADEs that could adversely affect the safety of participants.