Annex III

Conditions of the marketing authorisations

1. Conditions to be fulfilled by the MAH:

1. The MAH shall update the marketing authorisations of the affected dialysis solutions with the improved microbiological analytical methodologies and inclusion of new sites for increasing the diversity of supply in accordance with the change management plan and its timelines. Variations should be submitted for assessment by the national competent authorities.

2. The MAH shall perform a 12 month monitoring after site qualification by the supervisory authority (IMB) in Castlebar. Within 90 days of the finalisation of said monitoring period, a change management plan shall be submitted to the national competent authorities. The plan shall detail all changes to processes, frequencies or limits resulting from the monitoring.

3. The MAH shall draw up global corrective and preventive actions (CAPA) and use them to prevent endotoxin contamination at other sites producing dialysis solutions. The outcome of the global CAPA shall be provided to the national competent authorities and any changes considered necessary shall be addressed through the appropriate change management protocols and regulatory procedures at a national level, as applicable.

4. The MAH shall submit to the national competent authorities, at the time of the next Periodic Safety Update Report (PSUR), a risk management plan (RMP) for all affected products using the agreed consolidated RMP, version 2.0 of 21 September 2011, which describes the products' safety concerns (cloudy effluent/aseptic peritonitis with peritoneal dialysis solutions and endotoxin induced systemic inflammatory response with haemodialysis solutions) and their risk minimisation which includes a direct healthcare professional communication and quality activities. This RMP shall follow the EU RMP template (as referenced in Volume 9a of The Rules Governing Medicinal Products in the European Union) and shall include the measures to assess the effectiveness of the risk minimisation in the agreed consolidated RMP.

5. The MAH shall perform epidemiological studies consisting of a clinical audit that will collect data on the number of peritonitis events in the EU in 2010 and 2011 and an observational study to assess the nature of peritonitis and non-peritonitis cases (including fatal outcomes) and their outcome, in accordance with the milestones for evaluation and reporting described in the consolidated RMP.

2. Conditions to be implemented by the Member States:

1. The inspection of the Castlebar site by the supervisory authority (IMB) shall be performed by end of December 2011 before the solutions can be re-launched. The outcome of the inspection shall be provided to national competent authorities.

2. A pharmacovigilance inspection shall be carried out by the competent authority by end of September 2012. The outcome of the inspection shall be provided to national competent authorities.

3. During inspections of the local sites located under their territories, member states shall ensure that the MAH has appropriately transposed the experience acquired in Castlebar, in accordance with the global CAPA. Care should be taken to ensure consistency with the inspections of the Castlebar site. The outcome of the inspection shall be provided to national competent authorities.