

Mirandola, July 2016

Subject: Compatibility of INSPIRE oxygenator connected to Sorin Group Deutschland GmbH heater-coolers using hydrogen peroxide in the water path and circulating blood in the blood path

Dear Valued Customer,

With reference to the recent FSN issued by LivaNova on the "Use of Sorin Group Deutschland GmbH heater-coolers in combination with certain oxygenators with polymer heat exchanger designs", we provide here below the specific permeability rates of INSPIRE polymer heat exchanger oxygenator in relation to hydrogen peroxide.

As indicated in our Sorin Group Deutschland GmbH heater-coolers Operating Instructions, LivaNova directs customers to add hydrogen peroxide to the water of the device after the disinfection step. This process of adding hydrogen peroxide helps limit bacteria growth until the next water change and keeps it within the limits defined for drinking water quality standards. The specified concentration of hydrogen peroxide is 150 ml of medical grade 3% hydrogen peroxide added to the filtered tap water in the device, resulting in a maximum concentration of 330 ppm (equal to 0.033%) in the 3T and FlexTherm heater-cooler water circuits.

As communicated in the FSN, LivaNova's toxicological assessment has concluded that the Allowable Limit (AL) for hydrogen peroxide transferred to the blood during a typical bypass procedure not exceeding 6 hours is **0.21 mg/day per kg** of patient body weight, which practically means a limit of 12.60 mg/day for a 60kg adult patient. The quantity of hydrogen peroxide transferred to the blood circuit of an adult patient connected to an INSPIRE oxygenator was found to be **57 times below the Allowable Limit (AL)** over the duration of a 6 hours surgery procedure.

Sorin Group Italia S.r.l.
a wholly-owned subsidiary of LivaNova PLC
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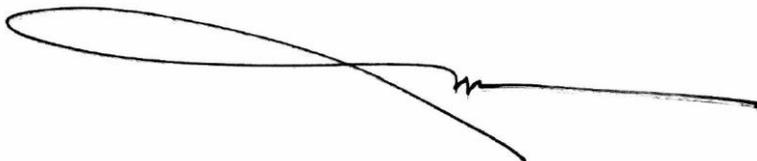
Capitale Sociale: € 8.550.034,00
Registro Imprese di Milano N. 10556980158
R.E.A. MILANO 1767776 – N.Mecc. Imp./Exp. MI 352423
Cod. Fisc. 10556980158 – Part. IVA 02109510368
ISO CODE IT02109510368
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Certain patient conditions may pose greater susceptibility to hydrogen peroxide, including but not limited to Vitamin E deficiency, certain heritable deficiencies of enzymes responsible for metabolism of hydrogen peroxide and related compounds, and certain haemolytic anemias. Our toxicological assessment concluded that use of the Sorin Group Deutschland GmbH heater-coolers in combination with INSPIRE, for durations of six hours or less, would not generate an unacceptable risk level for this group of patients.

Blood haemolysis during clinical use was also evaluated by connecting two simulated perfusion circuits to heater-coolers. Adult and small adult simulated perfusion circuits using the INSPIRE oxygenators were connected to heater-coolers with the recommended concentration of H₂O₂ on the water side. As a control, a small adult and an adult test circuits were also connected to a heater-cooler without H₂O₂ on the water side. Results of these in vitro haemolysis measurements for both the adult and small adult simulated perfusion circuits were found to be equivalent to the control test circuits.

We thank you for your attention to this matter. We invite you to contact your local representative for any further questions or concerns related to this information.

Sincerely,



Thierry Dupoux
VP, Quality Assurance and Regulatory Affairs
Cardiac Surgery Business Unit

IM-00689/A

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