CytoSorbents

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URGENT FIELD SAFETY NOTICE

CytoSorb® 300 mL Device

Potential incompatibility with Nitrous Oxide (N_2O)

December 22, 2015

Re: Customer notification concerning the CytoSorb® 300 mL Device

Dear Clinicians:

You are receiving this letter because our records indicate that you use the CytoSorb® 300 mL Device, a CE-marked extracorporeal cytokine adsorber intended for use in conditions where excessive cytokine levels exist.

The purpose of this Field Safety Notice is to inform you, out of an abundance of caution, of a possible incompatibility of the CytoSorb®300 mL Device with the inhaled anesthetic gas, nitrous oxide (N_2O). This combination has been associated with the death of three pigs in animal studies using the CytoSorb®300 mL Device for an intended purpose for which it is not yet CE marked. To our knowledge, there have been no such reported cases of adverse events relating to the combination of the CytoSorb®300 mL Device with nitrous oxide (N_2O) in treatment of humans.

CytoSorbents Inc. is a participant in an advanced military project conducted in the United States, where CytoSorb® 300 mL Device is being developed for new medical treatments that are not yet approved for human use. In recent related animal experiments, three intubated and sedated pigs, with pulmonary artery catheters in place, were anesthetized with a combination of nitrous oxide (N_2O) and oxygen (2:1), and isoflurane. These animals underwent extracorporeal circulation of their whole blood through a CytoSorb® 300 mL Device and two additional extracorporeal devices provided by another company, one of which was an experimental device. Set-up of the extracorporeal circulation access was unconventional (atypical clinical configuration), where blood was taken from a single port in a dual lumen catheter from the iliac vein, pumped through the cartridge systems using a development-stage pump system, and then back into the body through a single port of another dual lumen catheter placed in the jugular vein. Following the initiation of extracorporeal circulation, all three pigs developed both pulmonary and hemodynamic instability, resulting in the death of the animals (N=3) 11-15 minutes after the start of therapy. Another pig (N=1) was evaluated with the same experimental set-up, with isoflurane but without nitrous oxide (N_2O), and was stable throughout the entire extracorporeal blood purification procedure. CytoSorbents Inc. is working with the test facility to perform additional experiments to try to reproduce and determine the exact cause of the observed animal responses. Given the severity of the adverse event that occurred in these three test animals, and out of an abundance of caution, we wanted to notify all of our clinical centers of this observed

potential incompatibility of CytoSorb® 300 mL Device and the anesthetic gas, nitrous oxide (N_2O), as we continue our root cause analysis through additional animal studies.

Clinicians should not use CytoSorb in combination with Nitrous Oxide (N_2O) under any circumstances until we notify you otherwise. The clinical scenario we have described is likely to be most relevant for patients that are undergoing surgery using nitrous oxide (N_2O), which is relatively rare in modern surgical anesthesia.

The recommendation above does not apply to use of the inhaled pulmonary vasodilator, nitric oxide (NO) and CytoSorb® 300 mL Device, where no adverse events have been noted, for example, when used together with ECMO.

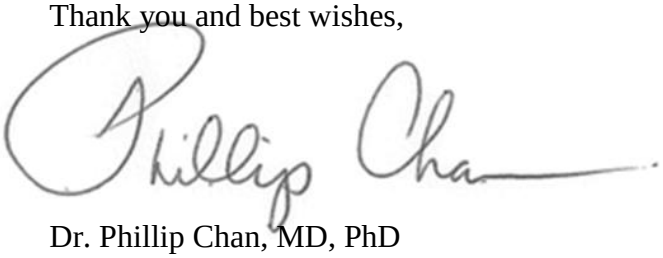
At CytoSorbents Inc., the safety of your patients is our primary concern, which is why we are rapidly informing you of these preliminary animal data. We would be grateful if you could pass this Field Safety Notice on to all those who need to be aware within your organization or to any organization where the CytoSorb® 300 mL Device may have been transferred. To acknowledge receipt of this Field Safety Notice, we would also be grateful if you could complete and return the enclosed response card. .

In accordance with applicable rules, the competent authorities in your country have been notified of this Field Safety Corrective Action.

Please contact Dr. Joerg Scheier, MD, our European Medical Director at Joerg.scheier@cytosorbents.com with any questions or concerns.

We are focused on delivering the highest level of product quality to you and appreciate your support. Your complete satisfaction is our top priority and we sincerely regret any inconvenience this may cause you.

Thank you and best wishes,



Dr. Phillip Chan, MD, PhD
Chief Executive Officer

URGENT Field SAFETY NOTICE
CytoSorb® 300 mL Device
Potential Incompatibility with Nitrous Oxide (N2O)
12/22/2015

Customer Name_____
Address_____
_____

I have read and understand the recommendation provided in the [*] December 2015 letter.

□ yes □ no

If you have experienced any adverse events associated with identified product, please explain and provide any additional information: _____

_____

Signature:
_____

Name/Title:
_____

Telephone: (_____)_____ Email address: _____

Please drop the postage paid card in the mail. Alternatively you can scan and send your response by

email to regulatory@cytosorbents.com or FAX +49 (0)30 654.99.146.

Alternatively Internet response may given at:

English: CytoSorb.com/reply-n2o
German: CytoSorb.de/reply-n2o

Your assistance is greatly appreciated