

# HemoDefend

Safeguarding the Quality and Safety of the Blood Supply



## Broad Removal of Blood Contaminants

to Improve Blood Quality and Reduce Transfusion Reactions

- Antibodies
- Free Hemoglobin
- Cytokines
- Bioactive Lipids
- Inflammatory Mediators
- Toxins
- Drugs
- Foreign Antigens
- Prions

## The availability of high quality and safe blood is essential

Nearly 10% of all US hospital admissions require a blood transfusion with 15 million packed red blood cell (pRBC) transfusions administered annually, and an estimated 50 million pRBC transfusions worldwide. Transfusion of platelets, plasma, cryoprecipitate and other blood products double this number. Trauma, surgery, critical care illnesses, cancer, military usage, and inherited blood disorders are just some of the drivers of transfused blood products. Despite advances in blood quality, there is significant room for improvement:

- **TRANSFUSION REACTIONS** - There is a low but tangible (1-4%) risk of non-hemolytic febrile and allergic transfusion reactions, undefined risks of allo-immunization, risk of atypical infection (e.g. prions), and risk of potentially fatal transfusion reactions including TRALI (transfusion related acute lung injury: 1 in 2,000 to 5,000 transfusions), anaphylaxis (1 in 20,000-50,000), angioedema, and hemolysis.
- **THE “OLD BLOOD IS BAD BLOOD” DEBATE** - Significant controversy surrounds the risk of “older” blood. Retrospective studies have linked old blood to adverse outcomes and an increased risk of death. This has spawned two randomized, controlled, prospective trials – RECESS and ABLE – to try to answer the issue. If these studies demonstrate an increased risk of old blood, more effective purification solutions will be urgently needed to avoid major blood shortages.
- **HIGH RISK PATIENTS** - Transfusion risk increases in patients receiving multiple pRBC units (e.g. trauma, surgery) and in “primed” susceptible patients (e.g. critical care and high risk surgery).
- **HIDDEN ECONOMIC COSTS** - In addition to the medical burden, transfusion reactions trigger substantial economic costs of treatment, investigation, and follow-up.

## Contaminants in blood cause transfusion reactions and adverse outcomes

Donated blood can contain foreign antigens, antibodies (e.g. anti-HLA, anti-granulocyte, IgA, anti-A, and anti-B), medications, infectious materials (e.g. prions, viruses) and other substances that can cause serious consequences. For example, TRALI is highly correlated with donor anti-HLA and anti-granulocyte antibodies, and is fatal up to 10% of the time. IgA can cause life-threatening anaphylaxis in IgA deficient hosts.

During blood storage, pRBC units also accumulate free hemoglobin due to hemolysis, and undergo in situ generation of bioactive lipids (e.g. lysophosphatidylcholine – LysoPC), cytokines, and other inflammatory mediators that can trigger transfusion reactions that vary in severity depending on the patient’s condition.

## HemoDefend - Safeguarding the quality and safety of the blood supply

HemoDefend is a powerful blood purification technology platform that removes antibodies, free hemoglobin, cytokines, toxins, drugs, bioactive lipids, and other inflammatory mediators from transfused blood products. Currently in advanced development, it is based on a very biocompatible, highly porous polymer bead technology. Each bead, roughly the size of a grain of salt, has millions of adjustable pores and channels in it, allowing it to capture and adsorb a wide range of molecules via pore capture and adsorption. “The end goal is to effectively “wash blood” without the expense, logistics, and time of actually doing so.” A version of these beads forms the basis of CytoSorbents’ flagship product, CytoSorb®, already approved in Europe as a first-in-class extracorporeal cytokine filter. HemoDefend may also be capable of removing prions, the infectious agent responsible for Creutzfeldt-Jakob, or “mad-cow”, disease.

Free hemoglobin reduction with HemoDefend (L) versus no treatment (R)



## HemoDefend - Works in two configurations: In-Line Filter & "Beads in a Bag"

Because HemoDefend beads form a low resistance, high flow matrix, it can be used as a dockable in-line filter between the blood bag and the patient. Added at the point of transfusion, the in-line filter can purify a unit of blood via gravity feed in less than 20 minutes. It is ideally suited for patients with a high risk of transfusion reaction, including those getting multiple units of blood and patients already primed for a transfusion reaction including critical care patients, and those undergoing high risk surgery.



Neutrally buoyant beads (R) vs normal (L)

In the unique "Beads in a Bag" treatment configuration, these beads are placed directly into a blood storage bag during bag manufacturing, with an integrated filter to prevent beads from leaving the bag during transfusion. During whole blood centrifugation and fractionation, packed red blood cells flow into the bag where the neutrally buoyant beads distribute automatically throughout the blood and immediately begin to remove contaminants from the blood without the need to mix or agitate. This continues throughout the entire blood storage period, maximizing removal efficiency and improving the quality of blood. Blood is transfused normally. Blood goes into the patient and the beads stay in the bag and are discarded.



## HemoDefend may help extend the life of fresh blood

Working in concert with blood preservatives that attempt to reduce reversible blood storage lesions, HemoDefend could help to purify the acellular component and offer a complete solution to help improve the chances that blood administered on Day 30 is as high quality as blood on Day 7.

## The HemoDefend technology platform is available for licensing

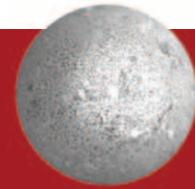
CytoSorbents (OTCBB: CTSO) is a publicly-traded medical device company working to save lives through blood purification. Through its HemoDefend

technology platform, CytoSorbents has developed a powerful and easy-to-use blood purification technology that can efficiently remove antibodies, free hemoglobin, cytokines, other inflammatory mediators, toxins, drugs and other contaminants from blood products during transfusion with the goals of:

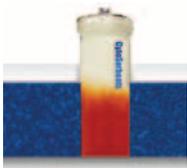
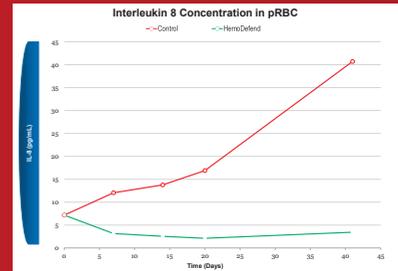
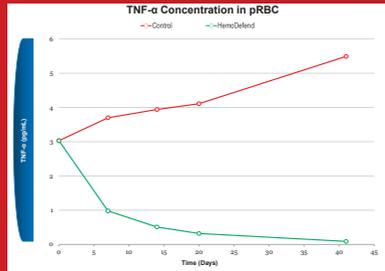
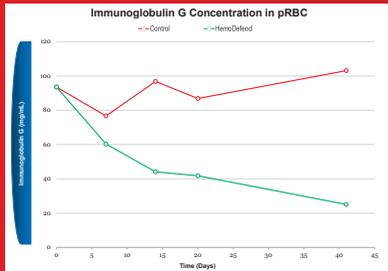
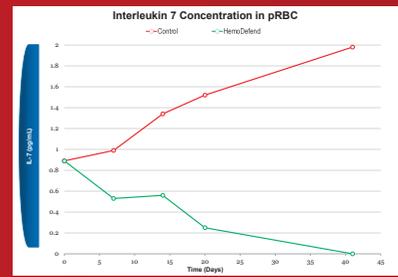
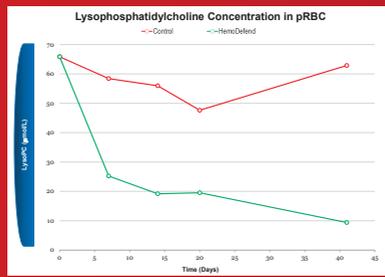
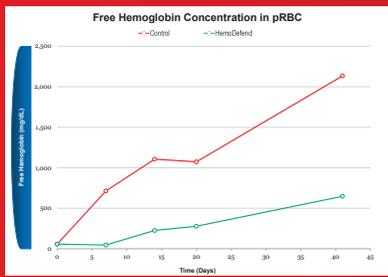
- Reducing life-threatening reactions such as TRALI and anaphylaxis
- Reducing nuisance transfusion reactions
- Maintaining the quality and safety of fresh blood
- Potentially extending the useful life of blood

The technology has the ability to convert a low margin, commodity blood storage bag into a higher margin, blood treatment system that can be used in mainstream, military and developing nation applications. CytoSorbents seeks to outlicense this technology to potential strategic partners and seeks additional military and government support. If interested in learning more about CytoSorbents and its technology, please contact CytoSorbents Corporation.

## HemoDefend Advantages



- **Highly biocompatible, meeting ISO 10993 standards** – Includes biocompatibility, hemocompatibility, acute toxicity, genotoxicity, cytotoxicity, and complement activation testing over 30 days
- **Ability to remove many contaminants that cause transfusion reactions** – Includes antibodies, free hemoglobin, cytokines, bioactive lipids, toxins, drugs and others
- **Can be used in multiple configurations including "Beads in a Bag"** – Dockable in-line filter is easy to set-up. "Beads in a Bag" requires no additional intervention and uses blood storage time to enhance contaminant extraction
- **Neutrally buoyant beads eliminates need for mixing** – Reduces risks of hemolysis or need for additional processing or equipment
- **One size need not fit all** – HemoDefend consists of a mixture of different beads with different capabilities to achieve broad spectrum removal of various substances. New capabilities can be easily added
- **No additional equipment, electricity or energy source needed** – Can be used in mainstream blood banking, for military applications in austere environments, in emerging countries with limited technology
- **Excellent capacity** – Massive surface area per unit mass
- **Easily sterilized** – Gamma and steam sterilizable
- **Long shelf life at room temperature** – Compatible with blood storage bag conditions
- **Inert material with no biologics, cells, ligands or drug components** – No perishable or leachable materials



# CytoSorbents

Working to Save Lives Through Blood Purification

To learn more, contact:

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**CYTOSORBENTS CORPORATION (OTCBB: CTSO)** is a critical-care focused therapeutic device company using blood purification to prevent or treat life-threatening diseases. Its purification technology is based on biocompatible, highly porous polymer beads that can actively remove toxic substances from blood and other bodily fluids by pore capture and adsorption. [www.cytosorbents.com](http://www.cytosorbents.com)

**HemoDefend** is a development stage product that is not yet approved in the United States or European Union. HemoDefend is currently available for licensing.