



# The Treatment of Dengue Hemorrhagic Fever

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## **Summary**

Dengue Virus and virulent Dengue Hemorrhagic Fever (DHF) represent an international health issue that remains untreatable with traditional antiviral drug and vaccine therapy. This document summarizes the application of the Aethlon Hemopurifier™ as a broad-spectrum therapeutic device able to clear dengue virus from infected patients, and potentially assist in the modulation of inflammatory cytokines associated with advanced DHF. The global prevalence of dengue has grown dramatically in recent decades. The disease is now endemic in more than 100 countries, and according to the World Health Organization, as many as 50 million cases of dengue infection occur each year.

## **Background of the Hemopurifier™**

Many viral pathogens, including Dengue, are not treatable with antiviral drug or vaccine therapy. When therapies do evolve, viruses often mutate to become resistant to treatment. Viruses that cross over from animal species into man compound the treatment challenge. Recent examples of such zoonotic transmission include HIV, SARS, West Nile, Ebola, Marburg, and most recently the H5N1 strain of Avian Influenza. Genetic modification of viruses with the intent to create drug and vaccine resistant bioterror threats minimize the likelihood that traditional therapeutics will keep pace.

The Aethlon Hemopurifier™ is a first-in-class device designed to fill the void in treating many drug and vaccine resistant pathogens. The technology promises to augment the benefit of drug therapy when available, and serves as a first line countermeasure in the absence of drug or vaccine treatments. The technology converges the blood filtration principles established in hemodialysis and plasmapheresis with the immobilization of affinity agents that capture envelope viruses by the surface carbohydrate structures they have evolved to evade the natural immune response. As a result, the Hemopurifier™ is able to reduce the body burden of infectious virus and related toxins, thus increasing the likelihood that a patient's own immune response can overcome infection.

Aethlon recently completed a 24-treatment safety study of the Hemopurifier™ in health compromised dialysis patients co-infected with Hepatitis-C virus. The study was administered at the Apollo Hospital in New Delhi, India. The resulting data has led to the submission of a preliminary Investigational Device Exemption with The Food and Drug Administration (FDA) related to the use of the Hemopurifier™ in the United States as a broad-spectrum countermeasure against class "A" bioweapon threats and pandemic influenza. Aethlon plans further clinical programs in India, and has initiated discussions with the Indian Council of Medical Research (ICMR) and other agencies related to the treatment of DHF and other viral conditions. In the capital city of New Delhi alone, 67 of the 2,640 persons known infected with Dengue since late July have died.

### **The Dengue Threat**

DHF is one of the greatest infectious disease threats known to man. DHF infection is transmitted through mosquito-borne Dengue viruses (serotypes 1- 4). The severe form of the disease, Dengue Hemorrhagic Fever – Dengue Shock Syndrome (DHF/DSS), is one of the leading causes of hospitalization and death among children in Asia, with the average case-fatality rate being approximately 17%.

Since the description of Dengue etiology in 1944, considerable effort has been put into vaccine development, with significant development challenges encountered. Included

among these challenges is the reality that Dengue virus infection of one subtype actually enhances the severity of disease caused by infection with another subtype. The first infection causes a relatively mild dengue fever. A subsequent infection, if it involves another subtype, causes DHF/DSS, while a third infection involving a third subtype, is almost always fatal.

In addition to the direct effects of the viral infection, advanced DHF can trigger viral sepsis leading to the overproduction of deleterious cytokines. Evidence also exists that alpha and beta interferon (IFN-alpha) and gamma IFN (IFN-beta) may be involved. As such, the development of an effective DHF treatment remains elusive.

### **The Hemopurifier™ as a Treatment for Dengue Hemorrhagic Fever**

The Hemopurifier™ has been designed to isolate and capture highly pathogenic viruses and emerging viral threats. At present, it represents the only proposed treatment for DHF that simultaneously targets broad-strain clearance of Dengue virus and also assists in the modulation of excessive cytokine activity. The deployment of the Hemopurifier™ as a treatment for DHF is consistent with Aethlon's corporate strategy to collaborate with government and corporate entities to develop the Hemopurifier as a broad-spectrum treatment for drug and vaccine resistant pathogens. Specific to DHF, the Hemopurifier™ serves as an extracorporeal method to augment the immune response, thereby improving the likelihood that the natural immune response can overcome infection. Attributes and considerations for deploying the Hemopurifier™ as a treatment for DHF, include:

- **Rapid Clearance of DHF** - The affinity agents immobilized within the Hemopurifier™ have broad-spectrum capabilities to capture envelope viruses by binding to glycosylated proteins that reside on viral surfaces. In the case of DHF, the virus capture is directed at surface glycoproteins, which are available binding sites, even in the case of viral mutation. In pre-clinical testing, the affinity agent immobilized in the Hemopurifier™ has demonstrated the ability to bind to a prominent Dengue surface protein. The ability to clear Dengue virus and viral fragments prior to cell and organ infection is likely to inhibit disease progression.

In regards to broad-spectrum capability, the Hemopurifier has demonstrated the capture of HIV, HCV, and Orthopox viruses related to human smallpox. Researchers at the National Cancer Institute (NCI) and the National Institutes of Health (NIH) have documented that the form of affinity agents immobilized in the Hemopurifier also have activity against other viral pathogens including Marburg, Ebola, and Influenza.

- **Broad Clearance of Cytokines** - The structure of the Hemopurifier™ provides for the potential to modulate the overproduction of deleterious cytokines. In fact, hemofiltration techniques have been indicated as an adjunct treatment for cytokine induced sepsis since 1990. As such, the Hemopurifier™ may be an ideal method to assist in cytokine modulation, as the pores of the Hemopurifier™ fibers are large enough to allow both cytokines and cytokine aggregates unable to be cleared in Hemofiltration, to be removed from circulation.

In closing, the Aethlon Hemopurifier™ offers to increase survivability of those afflicted with DHF. Seasonal epidemic outbreaks of Dengue are now underway in various regions around the world, including India, where the most serious resurgence of Dengue infection since 1996 is occurring. In the absence of a vaccine and effective antiviral drugs, Aethlon Medical will collaborate with the health agencies of governments that wish to advance the Hemopurifier™ as a treatment option for their citizens infected with DHF.

### **About Aethlon Medical**

Aethlon Medical has developed the first-in-class medical device to treat infectious disease. The device, known as the Hemopurifier™, is a broad-spectrum treatment countermeasure against drug and vaccine resistant bioweapons, naturally evolving pandemic threats such as H5N1 Avian Flu, and chronic infectious disease targets including Hepatitis-C (HCV) and the Human Immunodeficiency Virus (HIV). Global researcher, Frost & Sullivan, recently awarded the Hemopurifier™ the 2006 Technology Innovation Award for its advances in the field of biodefense. Aethlon has also initiated research on a second generation Hemopurifier™ that targets the capture of growth factors

inherent in the spread of Cancer. More information on Aethlon Medical and the Hemopurifier™ technology can be found at [www.aethlonmedical.com](http://www.aethlonmedical.com).