



## **H-BAC Thromboresistant Heparin Coating Solution Frequently Asked Questions**

### **How long does the H-BAC coating remain effective once applied to the device?**

The H-BAC coating is not chemically bonded (e.g., not covalently bound) to the surface of the medical device, so environmental influences at the site of use will influence the duration of effectiveness. The duration of the antithrombogenic effectiveness of the H-BAC coating on the specific medical device to which it is applied is directly proportional to where and how the device is used. If the H-BAC coated device is placed in a rapidly moving stream of blood, such as might be expected with a percutaneous transluminal cardiac angioplasty (PTCA) catheter, the effectiveness of the H-BAC coating is the shortest at just over 24 hours. But H-BAC coatings on PTCA catheters is widely used because the duration of use of such a catheter is usually less than five hours, and the antithrombogenic effect of the H-BAC coating is very useful in helping prevent clots from being formed on an otherwise un-coated device. If the H-BAC coated device is placed in a very slow moving source of blood, then the effectiveness of the H-BAC coating is much longer and can be measured in days rather than hours.

### **How does H-BAC react with stainless steel?**

Every product has different "wettability" characteristics that are important when considering H-BAC deposition onto the device. In our experiences, stainless steel is an acceptable surface for an H-BAC coating. Many guidewire manufacturers use H-BAC coating to help prevent against clot formation.

### **Will current laboratory test methods still be applicable once the H-BAC has been applied to the device or do different test methods need to be used?**

If you would please provide a NAMSA technical expert with details regarding what specific tests you now perform, we would be happy to try to address any concerns you have about how H-BAC may affect those test methods/results. For example, if you are now performing a bioburden test by performing a saline wash followed by a plate count, the waxy H-BAC coating may prohibit the saline from removing microorganisms; it may be appropriate to test uncoated as well as H-BAC coated devices to demonstrate equivalence.

### **What kind of shelf life is expected once H-BAC is applied to our device?**

Shelf life of the un-used H-BAC coated product should be the same as the device itself. However, a similar thought process and testing program should be used to document shelf-life of the H-BAC coated device.

### **How is H-BAC applied to my device?**

A simple dipping of the product (e.g., stainless steel spring) in H-BAC followed by air drying (allowing the isopropyl alcohol carrier to evaporate) is sufficient to coat the device. H-BAC may be diluted with isopropyl alcohol (USP) if a weaker H-BAC solution is desired (simple tests such as the In Vitro Plot Clot method for determining thromboresistance may be performed to determine efficacy of the H-BAC coating).

### **Does NAMSA offer any specific services to characterize the H-BAC coating on my medical device?**

In addition to the standard biocompatibility testing services that NAMSA offers for all medical devices, which may be necessary to characterize your H-BAC coated device, we offer a couple of specific services to characterize the efficacy of the H-BAC coated medical device:

- 1) Plate Clot Method for Thromboresistance (In Vitro), NAMSA Test Code V12-00, 2) – This procedure is used to screen the efficacy of the H-BAC coated device. Test (H-BAC coated) and control devices are placed in direct contact with freshly drawn, uncoagulated rabbit blood. The test system is observed for clotting at the blood-material interface. Test articles are compared with positive and negative control materials, known to resist and promote clotting, respectively.
- 2) Heparin Activity Assay, NAMSA Test Code (to be determined) – This ELISA procedure is used to quantitate the heparin activity present on the surface of an H-BAC coated device.
- 3) Cytotoxicity, NAMSA Test Code V0010-110 USP Agarose Overlay Method, Direct Contact and V0015-110 ISO Agarose Overlay Method, Direct Contact – These cytotoxicity assays are used to evaluate the potential for H-BAC coated devices to exhibit cellular toxicity when in direct contact with L929 mouse lung fibroblast cells.
- 4) Hemolysis, NAMSA Test Code V0019-100 In Vitro Hemolysis, Modified ASTM, Direct Contact – This hemolysis test is used to evaluate the potential for H-BAC coated devices to result in the hemolysis of red blood cells when in direct contact with rabbit blood.

### **Does H-BAC exhibit cytotoxicity and hemolytic activity?**

Heparin is combined with benzalkonium chloride to create H-BAC. In undiluted concentration (800-900 heparin units per mL), H-BAC coated devices have been observed in many instances to cause cytotoxic and hemolytic activity. Part of this activity is related to the wettability of the medical device onto which the H-BAC coating is applied (every type of material exhibits a different level of wettability resulting in a different degree of H-BAC coating thickness to that device).

The cytotoxic and hemolytic activity of H-BAC is believed due to the BAC (benzalkonium chloride) portion of the H-BAC moiety. Benzalkonium chloride is a detergent and detergents are known disruptors of cell membranes (e.g., L929 mouse lung cells used in cytotoxicity and red blood cells used in the hemolysis test). It is not free benzalkonium chloride present in H-BAC solution that is believed to cause this activity because we test for free benzalkonium chloride and none present in the H-BAC solution. The cytotoxic and hemolytic activity in H-BAC is believed due to the benzalkonium chloride that is attached to the larger heparin moiety (heparin has a size of about 45,000 daltons). H-BAC can be diluted such that the device can still be coated with an effective Thromboresistant layer of H-BAC (as demonstrated by the In Vitro Plot Clot Method), and at some point (depending in part on the wettability of the device) the cytotoxic and hemolytic activity is observed to disappear. The trick is to find the balance between an H-BAC coating resulting in effective thromboresistance and the resulting elimination of the cytotoxic and hemolytic activity. Some clients prefer to rely on other tests such as the rabbit muscle implant test and the rabbit intracutaneous study to demonstrate the biocompatibility of the H-BAC coating, and explaining the cytotoxic and hemolytic effects as being due to the presence of the benzalkonium chloride in H-BAC (the uncoated device can be tested simultaneously to show no cytotoxicity and no hemolytic effects).

**Medical Engineering Technologies Ltd.**

**Webster House, Jesmond Street, Folkestone, Kent CT19 5QW, UK.**

**Tel: +44 (0)8454 588924 Fax: +44 (0)8700 562153 E-mail: [solutions@met.uk.com](mailto:solutions@met.uk.com)**