

## Hibernation Therapeutics USA, LLC

*Innovations from Nature to Medicine*

Information Contained herein is Strictly Confidential and  
intended for education and informational purposes of the recipient ONLY

### **IMPORTANT INFORMATION**

The formulation and use of the patented *Adenocaine™ Technology* requires a license from Hibernation Therapeutics Global, Ltd. Any unauthorized use of the technology is prohibited and will be considered willful infringement of the patents.

Registered To: \_\_\_\_\_

# **GUIDELINES FOR THE USE OF ADENOCAINE™ ALL-BLOOD CARDIOPLEGIA FOR ARREST MAINTENANCE AND REANIMATION**

*"Despite continuous improvements in surgical technique and cardioplegic formulations, the inadequacies of current intraoperative protection protocols and formulations, most of which contain as their basis high potassium depolarizing arrest, remain a concern."*

James D. McCully JTCVS (2002)<sup>1</sup> p. 219-20.

#### **For information please contact**

Hibernation Therapeutics USA, LLC  
487 Cherry Street  
Third Street Tower  
Macon, GA 31201  
[www.Adenocaine.com](http://www.Adenocaine.com)  
(o): 478-744-9994  
(f): 478-744-9996

*The information contained in this document on all-blood cardioplegia is intended exclusively for use with the Quest MPS® Microplegia System (Quest Medical, Inc. Allen, Texas, USA). The terminology used is consistent with the MPS® components and consumables (see <http://www.questmedical.com/products/mps.asp>). A separate Hibernation Therapeutics Global, Ltd. Educational Guidelines document is being prepared for blood:crystalloid or all-crystalloid cardioplegia formulations using the Adenocaine™ technology. See page 3 for Hibernation Therapeutics Global, Ltd. Disclaimer of Liability.*

# Hibernation Therapeutics USA, LLC

Innovations from Nature to Medicine

Information Contained herein is Strictly Confidential and  
intended for education and informational purposes of the recipient ONLY

## **TABLE OF CONTENTS**

<b>Disclaimer of Liability</b> .....	3
<b>Adenocaine™ Arrest Induction, Maintenance and Reanimation</b> .....	4
• Chemicals	
• <i>Filling the ARREST and ADDITIVE Cassettes</i>	
<b>QUICK START: Arrest Induction, maintenance and reanimation</b> .....	5
• <i>Adenocaine™ “polarized” Arrest Maintenance and Reanimation</i> .....	6
• <i>Frequently Asked Questions and troubleshooting</i>	
• <i>Arrest Induction</i> .....	6
• <i>Maintenance</i> .....	7
• <i>Reanimation</i> .....	8
• <i>General Questions</i> .....	12
<b>DETAILED INSTRUCTIONS for Delivery of Adenocaine™ All-Blood Microplegia</b> ....	16
<u><b>Phases of Cardioplegia using Microplegia</b></u>	
• <i>ARREST “INDUCTION” 15 mEq K<sup>+</sup>/L assisted Adenocaine™</i> .....	16
• <i>ARREST “MAINTENANCE” Adenocaine™ with ~2 mEq/L K<sup>+</sup></i> .....	17
• <i>REANIMATION Adenocaine™ with ~0 mEq K<sup>+</sup> (rely on blood K<sup>+</sup>)</i> .....	18
<b>BACKGROUND: Adenocaine™ Arrest Induction, maintenance and reanimation</b> ...	19
• <i>Addressing an Unmet Medical Need</i> .....	19
• <i>Scientific Background</i> .....	19
• <i>Lessons from Natural hibernators in Service to Cardiac Surgery</i> .....	21
<b>DEFINITIONS, DRUG PROPERTIES AND USE IN CARDIAC SURGERY</b> .....	22
• <i>Miniplegia (or Microplegia™)</i> .....	22
• <i>Depolarized and Polarized Cardioplegic Arrest and Maintenance</i> .....	22
• <i>Adenosine</i> .....	23
• <i>Lidocaine-HCl</i> .....	25
• <i>MgSO<sub>4</sub> 7H<sub>2</sub>O</i> .....	26
• <i>Adenocaine™</i> .....	27
<b>APPENDIX 1. Key background Pre-clinical and Clinical Scientific Abstracts</b> .....	28
• <i>Adenosine</i> .....	28
• <i>Lidocaine</i> .....	33
• <i>Adenosine and Lidocaine</i> .....	40
<b>APPENDIX 2. About Hibernation Therapeutics and its Patent Portfolio</b> .....	46
<b>APPENDIX 3. Research Publications relevant to Hibernation Therapeutics</b> .....	47
<b>APPENDIX 4. FDA Approved Indications of Adenosine and Lidocaine</b> .....	48
<b>REFERENCES</b> .....	49

## Hibernation Therapeutics USA, LLC

*Innovations from Nature to Medicine*

Information Contained herein is Strictly Confidential and intended for education and informational purposes of the recipient ONLY

**Disclaimer of Liability:** The document is intended as guidelines for use of the Adenocaine™ technology obtained from published and unpublished pre-clinical sources and clinical cases, and from practices currently using the technology in cardiac surgery. In preparing of these guidelines, every effort has been made to offer the most current, correct, and clearly expressed information possible. The guidelines have undergone a thorough review; nevertheless, inadvertent errors in information may occur. In particular, and not limited to, Hibernation Therapeutics Global, Ltd. (“HTG” or “Company”) parent company or any of its subsidiaries disclaims any responsibility for typographical errors affecting the accuracy of the information that may be contained in the document, or any adverse events that may arise or occur from using the information contained in this document. The Company suggests that any use made of the technology based on information included in these guidelines be subject to scientific and educational consult with the Company. The Company makes no representations or warranties regarding the functionality of this information or its suitability for use including any direct, indirect, punitive, special, incidental, or consequential damages.

HIBERNATION THERAPEUTICS GLOBAL, LTD MAKES NO REPRESENTATIONS OR WARRANTIES OF ANY KIND IN THE DOCUMENT AND ALL OTHER WARRANTIES, EXPRESS OR IMPLIED, INCLUDING, WITHOUT LIMITATION, IMPLIED WARRANTIES OF SAFETY, MERCHANTABILITY AND FITNESS FOR A PARTICULAR PURPOSE, US FDA REGULATORY APPROVAL AND NON-INFRINGEMENT ARE EXPRESSLY EXCLUDED FROM THIS AGREEMENT.

Hibernation Therapeutics Global, Limited or any of its subsidiaries further acknowledges and hereby gives notice that certain suggestions in the guidelines may be subject to change based on individual patient needs and surgeon preference.