

# Preface

It has been a while since a comprehensive review of the status of Hemoglobin-Based Oxygen Carriers (HBOCs) has been assembled. Indeed, the field in many ways has become orphaned as clinical and technologic advances in blood banking and the management of anemia move forward. Spurred on in the early 1980s with the onset of AIDS, HBOC development was rich and productive, an alternative to risky red cell transfusions. This led to a more modern approach to red cell transfusion and HBOCs were more or less relegated to specific applications as “oxygen therapeutics”. All the while of course, there continued a need for an oxygen therapeutic if only for use when blood was neither an option nor available. Clinical trials with a number of HBOCs went forward and all failed to produce results sufficient to permit FDA regulatory approval. In the early part of the current century it appeared as if there was no need for such a product and the regulatory environment continued to be challenging.

We decided to bring the field up-to-date with the construction of this book. Dedicated to HBOCs alone, our intention was to bring together in one place the current status of the field, a starting point for those interested in joining in on the adventure of discovery, a place for the veterans of the fight to read and reflect on what was and thinking about creating “what can be”. We hold that there continues to be a need for an oxygen therapeutic and that need can be met successfully with a HBOC. In fact, there is an urgency to develop HBOCs as an alternatives to donor blood for transfusion. Based on current world demographics, it has been predicted that, in coming decades, there would be a serious shortage of transfusable blood because of higher demands due to rapidly aging populations in many countries while relative decrease in eligible younger donors.

The organization of this work is rather traditional, starting with an historical overview and statement of scientific principles as the foundation for the products. Moving onto a specific application in hemorrhagic shock is a natural development as in addition to AIDS, it was and remains a clearly stated potential application. A discussion of some of the current issues and regulatory framework rounds out the establishment of a foundation for the rest of the book.

A rather large section discussing many of the newer and older approaches to HBOC development follows. Here, the many different ideas for resolving some of the questions posed by regulatory and experiential reports are addressed creating a plethora of new modifications and processes as they move along. Clearly, the next

step is to identify and catalog the potential applications for these products. While the universe of potential applications exceeds those presented here, these are but a few specifics linked to unique HBOCs. There are many more possible, a near endless list could be generated.

There follows a section on preclinical evaluation, a critical step in the regulatory process. Here again, generalizations from specific applications and products form the reference model. In the background remains the issue of how appropriate and useful are animal models in the development of human-use products and we are aware of many HBOC preclinical studies that may not be relevant to how humans will respond to the product given the variation in human physiology and disease state.

As the failure of clinical trials has been the major blockade to regulatory approval it seems appropriate to include commentary on this issue. There are critical questions posed in these writings that should be considered when contemplating HBOC clinical trials. As a corollary to a discussion of clinical trials, a section on the adverse events so critical to gaining an understanding of how they come about and more importantly how they can be mediated or prevented is a logical follow-on.

We think this discussion is critical to understanding how HBOCs work, how their use to date in general, and in trials specifically as well as in compassionate use situations. There are many reasons for an adverse event to appear and it is not always clear in the rigid analysis of data from a randomized trial that the HBOC is responsible for the observation.

To that end, we conclude with a white paper that proposes a consortial approach to facilitate development of safer and more effective HBOCs. A HBOC research consortium composed of committed independent investigators would allow objective investigations of critical issues based on unbiased scientific principles and methods.

This book is meant to bring an up-to-date perspective to the HBOC field, a reference for where the field stands at this point in time. It is our sincere hope that it accomplishes this objective and meets your specific needs.

Sincerely,

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