

Book Review

Injectable Dispersed Systems, Formulation, Processing and Performance **Edited By Diane J. Burgess,** **Published by Taylor and Francis Group,** **Boca Raton FL, 2005** **ISBN 0-8493-3699-6**

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This latest textbook in the “Drugs and the Pharmaceutical Sciences” series aims at providing in-depth information on injectable suspensions and emulsions, delivery systems which are becoming more common, in particular, for biologics, gene therapy, and some small-molecule low-solubility drugs. Indeed, this 644-page book, which encompasses all dispersed systems from simple suspensions and emulsions to more complex systems such as liposomes and microspheres, includes a wide range of information related to formulation, scale up, characterization, testing, and regulatory registration. The book is structured in four sections: Section I is an overview of basic principles of formulation and characterization; Section II reviews formulation aspects of the various systems; Section III is a series of case studies related to the development of specific products; and Section IV deals with quality and regulatory issues. This book review is written from the perspective of an analytical scientist and focuses principally on three chapters that specifically deal with the development of in vitro release tests for the evaluation of the release profile of injectable suspensions and the development of IVIVC.

I found the general chapters in the first section to be very well written and informative. The theoretical background in Chapter 1 is easy to follow and well supported by references. Chapter 3, which gives an overview of characterization and analysis techniques, will be of particular interest to analytical scientists who are new to dispersed systems, as it describes in some detail techniques that are useful for the characterization of the whole system as well as the individual particles, information each technique can provide, their utility for monitoring physical stability of suspensions, and possible pitfalls in interpreting results. Chapters 4 and 5 deal with in vitro–in vivo release considerations, a critical aspect of development of dispersed systems that are designed to release the active ingredient over a more-or-less prolonged period. Chapter 4 describes the applicability

of existing dissolution apparatus to injectable formulations and the various approaches published to date for such products. A variety of approaches based on either diffusion through membranes (i.e., two-compartment models) or on “sample and filter” techniques (i.e., any techniques that involve mixing of the test formulation in the dissolution medium and sampling at pre-set timepoints, including flow-through systems) are described and abundantly backed by references, giving a good overview of the options available. Some approaches are explained succinctly, but others are presented in more detail, with schematics of the apparatus. One can regret that the authors did not discuss in more depth the development of “accelerated” in vitro tests as an alternative to “real-time” tests for formulations designed to release over days or weeks. Very little guidance is actually given on modifying the experimental conditions to achieve a suitable in vitro release in a reasonable time frame. The second part of the chapter provides information on the in vivo release, with discussions on the animal model and dose volume considerations. The chapter on in vitro–in vivo correlations (Chapter 5) is complex and may not be an easy read for those who are not familiar with the mathematical models and computer programs designed to model drug release. Of more general interest is the part of the chapter that explains some of the issues encountered in developing IVIVC’s for injectable systems, in particular adjusting the model for the time differential that may exist between the in vivo release and the in vitro release.

Section II comprises four chapters on design and manufacturing of the principal categories of dispersed systems, namely coarse suspensions, emulsions, liposomes, and microspheres. I cannot comment on the relevance of the information provided to a formulator but found these chapters of interest to anyone who is involved in the development of such a system and wants to understand more

about excipient selection, importance of process parameters, release mechanisms, stability problems, and characterization. The chapter on liposomes is particularly instructive and readable. The only disappointment overall is that process scale-up is hardly discussed in these chapters, and readers interested in manufacturing will have to turn to the case studies (Section III) for discussions on this topic.

The third section is a compilation of nine case studies. It is unusual to find case studies in a textbook, and one wonders why this editorial choice was made. Nevertheless, these individual articles serve as a complement to the general chapters by providing a practical viewpoint on the subject. As mentioned above, many of the examples that deal with formulation development provide more specific observations regarding technology transfer and scale up, which were somewhat overlooked in the general chapters. Among the nine case studies, Chapter 17 illustrates the use of in vitro–in vivo release in the development of an injectable microsphere formulation. The chapter gives an essentially chronological recount of method development. Even though the structure of the text is more that of a technical report than of a scientific article, it illustrates well how analytical method development must proceed in parallel with formulation development. In this case, a simple in

vitro test (suspension of one unit dose in phosphate buffer saline dissolution medium followed by sampling at predetermined timepoints, with medium replacement) was used in the initial phase of development. Once several prototypes with different burst effect in vivo became available, a two-compartment test system based on dialysis was developed and used to generate preliminary in vitro–in vivo correlations. This chapter also describes the characterization of the microspheres using electron microscopy and various spectroscopic techniques during the in vitro release to monitor what structural changes are happening as the drug is released from the microspheres.

The final section of the book addresses quality and regulatory issues related to the development of injectable dispersed systems (Chapter 19) and liposomes and microspheres in particular (Chapter 20). These two chapters do not stray from very general considerations and, as such, are somewhat weaker than the rest of the book.

Overall, *Injectable Dispersed Systems* reaches its goal to be a comprehensive resource on all aspects of design, processing, testing, and registration of these complex formulations. With its wide scope and up-to-date bibliography, it will provide a starting point for scientists who are new to the field and a useful reference for those more experienced.