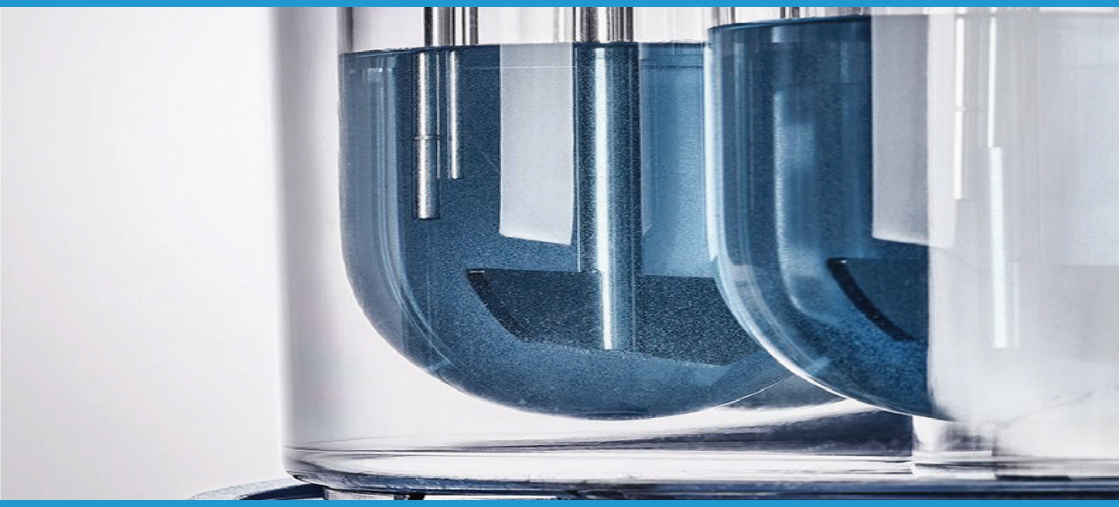
Desk Book of Pharmaceutical Dissolution Science and Applications

Second Edition, Revised and Updated



Editors:
Sandip B. Tiwari
Umesh V. Banakar
Vinod P. Shah

Society for Pharmaceutical Dissolution Science (SPDS)

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Introduction

Society for Pharmaceutical Dissolution Science (**SPDS**) was formed on 16th July 2012 at Mumbai, India with the objective of promoting the science and technological development in the field of dissolution testing among pharmaceutical professionals from industry, academia and regulatory bodies. The vision and mission statement of SPDS is noted below

Vision

To be as one of the most prominent professionals body focusing on dissolution science among the pharmaceutical industry and academia

Mission

To dissipate the science and advancement taking place in the field of dissolution related to clinical application and methods.

The First Edition of the *Desk Book of Pharmaceutical Dissolution Science and Applications* was well received by pharma researchers and had a positive feedback from the users. With many advances taking place in the field of dissolution science it was decided to bring out the Second Edition of the book with additional information on Dissolution Science and Application. With contributions from expert scientists across the globe on the subject matter, SPDS is bringing this Second Edition of the *Desk Book of Pharmaceutical Dissolution Science and Applications.* The aim is to provide the academia industry and research scientists in general an overview of basics fundamentals in the dissolution science and testing, recent developments in instrumentation and automation, changing regulatory requirements and innovations in the area of dissolution science and dissolution/*in vitro* release for novel dosage forms. The chapters provide details about the instrument operation, tips to overcome problems in design and development with adequate literature citations. The chapters also reveal methods of statistical analysis and interpretation of dissolution test data, application of data in terms of correlation with bioavailability and bioequivalence. The new and revised chapters discuss the role of solid-state properties, role of excipients and use of biorelevant media, role of dissolution in nutraceuticals and natural products and role of dissolution/drug release in regulatory applications towards biowaiver. This is a unique book of its kind, providing sound knowledge of scientific principles of dissolution and its applications.

We look forward to your contribution to SPDS's endeavour to bring best in dissolution technologies to the researcher in the field and enhance understanding of the subject.

L. Ramaswamy, Ph.D.
General Secretary,
SPDS, Mumbai, India

Preface

The roots of *in vitro* dissolution testing can be traced to late 19th century. The progression in the understanding of the science involved in solubility-based dissolution process and its applications over 130+ years has found a firm footing in drug development process and various allied disciplines associated within it, especially, in defining and establishing the quality attributes of a pharmaceutical product and its performance, both *in vitro* and *in vivo*. As a result, dissolution testing has emerged as a regular quality control procedure in good manufacturing practice. Whether or not its numbers have been correlated with biological effectiveness, the standard dissolution test is a simple and, perhaps, an inexpensive indicator of the physicochemical consistency of the product. As of date, *in vitro* dissolution tests seem to be the most reliable predictors of *in vivo* availability. Although official tests have great practical value, the fact that there is still a need for a test more directly related to bioavailability has been recognized.

Despite the accumulation of a massive body of information and data relating to the various aspects of dissolution test(ing), the pursuit to accurately predict *in vivo* performance continues unabatedly even today. The array of attempts – Biopharmaceutics Classification System (BCS), Topical Drug Classification System (TCS), *in vitro* release testing (IVRT), *in vivo* permeation testing (IVPT), physiological based pharmacokinetic modeling (PBPK), development of 'more' bio-physiologically relevant dissolution test, proliferation and marketing of bioavailability predictive software(s), drafts and innumerable revisions of regulatory guidances and/or recommendations from regulatory agencies across the world, are but a few of the many attempts that are being embarked upon in this pursuit. The net outcome from these attempts has resulted in the realization that *"the more we learn, the less we know!"*

While a solution to this pursuit appears to be beyond reach, at the present time, the more recent foray of *in vitro* dissolution testing has been realized in development of new drug products via 505(b)(2) new drug application (NDA) route, in development of nutraceuticals and natural products, development of biosimilars, among others. It is amply evident and clear to those that have a longstanding as well as continued involvement in *in vitro* dissolution test(ing), that the science and applications of dissolution test(ing) in all aspects of the life cycle of a drug product are still evolving and maturing.

It was our privilege to bring forth the first edition of this text in 2015. Now it is our pride to present to you the second edition. The intention of this desk book (2nd edition) continues to present a comprehensive mass of critical information, as a ready reference, to the R&D (formulation and analytical), QC/QA and PK professionals concerning the science and applications of effective dissolution testing and its utility in drug development. In addition to the topics addressed in the 1st edition, the role of dissolution test(ing) in development of new drug products via 505(b)(2) NDA, in development of nutraceuticals and natural products, role of solid-state properties, role of excipients and use of biorelevant dissolution media, use of dissolution test for biowaivers,

among others, have been included. As a result, this text should be considered in conjunction with the first edition to gain a comprehensive and wholistic understanding of the science and applications of dissolution test(ing).

The editors: Sandip B. Tiwari, PhD (SBT), Umesh V. Banakar, PhD (UVB) and Vinod P. Shah, PhD (VPS), are indebted to the authors for their contributions to this desk book. Additionally, the editors would like to thank the Society for Pharmaceutical Dissolution Science (SPDS) for its support in bringing forth this textbook. Furthermore, the editors express gratitude to Ms. Bhakti Poonia of Sotax India Pvt. Ltd., and Mr. Tarun Soni of NIC Interactive, the printers and publishers of this desk book for their expeditious and timely support. Special thanks are extended to L.Ramaswamy, PhD, General Secretary, SPDS for his unwavering support and encouragement through all the phases of this project. Last, but not the least, the editors would like to thank all the well wishers for their support that is often taken for granted, however, needs to be recognized.

Sandip B. Tiwari, PhD
Umesh V. Banakar, PhD
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Forward

Society for Pharmaceutical Dissolution Science (SPDS) is the first and only professional organization entirely dedicated to understanding and advancement of dissolution science. It was created to promote and update the development of science and technology in dissolution among the pharmaceutical professionals and academia. It provides an ideal platform to discuss the advances in dissolution science.

The Vision of SPDS is to be one of the most prominent professionals body focusing on dissolution science, and its mission is to dissipate the science and advancement taking place in the field of dissolution related to clinical applications and methods.

Dissolution testing over the last half century has emerged as a highly valuable *in vitro* test to characterize the drug product performance. Increasingly *in vitro* dissolution testing is relied on to assure product performance. While traditionally developed for solid oral dosage forms, the use of dissolution / drug release testing has been widened to a variety of novel dosage forms such as transdermals, semi-solids, liposomes, parenteral preparations and now nutraceuticals. Scientifically, a lot of progress has been made in the area of dissolution / drug release over last few decades.

Dissolution testing is currently enjoying a resurgence of interest on academic as well as on industrial and regulatory levels. The groundwork should continue to be focused on the development of dissolution tests and testers that are both biorelevant and can be adapted to routine quality control. To further improve the predictive capability of dissolution testing, there needs to be further refinement of the dissolution media and use of appropriate hydrodynamic designs that can better model flow patterns in the gut. It is likely that dissolution testing will become an even more powerful tool for the assurance of product quality, in the broadest sense in the years to come.

Various chapters included in this Desk Book include historical highlights, dissolution science and its impact on bioavailability, factors affecting dissolution, selection and influence of the dissolution media, qualification and validation of dissolution equipment, and automation are all aimed at providing practical insight that needs to be considered when developing a dissolution / drug release test. The general chapters also discuss compendial requirements and how to deal with “out of specification” dissolution results. Dissolution testing has gone beyond the tablets and capsule dosage forms, it now covers novel dosage forms such as transdermals, semisolids such as cream, ointment and gel, liposomes, parenterals, nutraceuticals and natural products. These advances need a good scientific base, good discussions and deliberations, and SPDS provides an ideal platform for this.

A discussion forum for all the scientific, regulatory and practical application aspects in the field of dissolution / drug release is the best way to keep the dialogue running and to allow us to continue to make progress. SPDS is a very valuable forum in this regard.

The second edition of the Desk Book includes updated and new chapters related to the application of dissolution science including regulatory applications of biowaiver.

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**Deceased at the time of publication. The Editors acknowledge the contributions of Prof. Gohel and Prof. Constantin to the Deskbook and pray to almighty to give eternal peace to the departed soul.*

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