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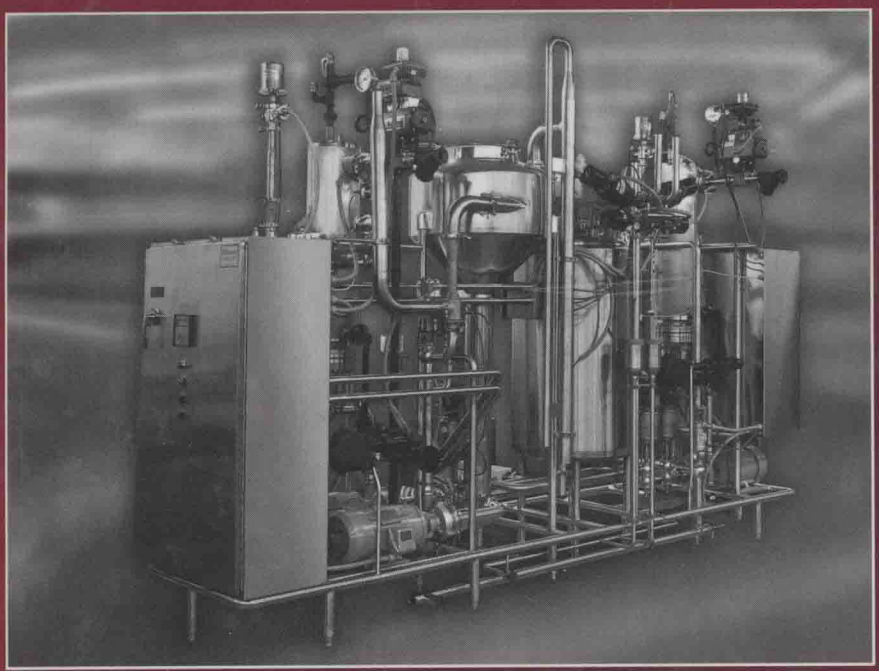
Clean-In-Place for Biopharmaceutical Processes



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Clean-In-Place for Biopharmaceutical Processes

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Preface

Clean-in-Place for Biopharmaceutical Processes is intended to be a source of information for personnel from all disciplines who are involved in the manufacture of a pharmaceutical product—from the scientist who creates the drug to those responsible for the design, construction, validation, and operation and maintenance of a facility, as well as for those responsible for regulation.

The objective of this book is to combine the experience and knowledge of experts familiar with the many items of equipment required for the pharmaceutical process with the knowledge of people who have had long experience in the successful application of clean-in-place technology to a variety of non-biopharmaceutical and biopharmaceutical processes. The unit operations of the process are analyzed with respect to whether or not clean-in-place is a possible or preferred method of cleaning, and examples of successful applications are included. While each new user of clean-in-place has a tendency to "reinvent the wheel," this book is an attempt to show that, for the most part, there are no new problems; rather there are problems solved previously, in a different application. However, considerable effort has been made to recognize and define innovative and emerging technology. The established criteria for successful clean-in-place is well defined, explained, and illustrated. A major goal of this book is to guide all readers to the development of the need for *clean-in-place* rather than *clean-in-part*.

Clean-in-place technology has been developing constantly for more than 50 years in dairy, beverage, and food applications for cleaning processes that produce fluid, semi-fluid, and dry granular products. Early development in these industries was generally guided by a small group of user personnel with intimate knowledge of the chemistry, bacteriology, and cleaning needs of the product, who were willing and able to seek outside support regarding the application of developing clean-in-place technology, sometimes referred to as "in-place cleaning" or "recirculation cleaning" in early literature. Much of the technical know-how was acquired during the early period of retrofitting clean-in-place to existing processes, primarily in dairy and brewing applications. A few well-qualified vendors of clean-in-place systems, sprays, and associated components served the needs of the entire market with "off-the-shelf" components and systems that were quite similar in the operating characteristics of flow and pressure. The regulatory agencies concerned with the application of this new technology were participants in the projects and members of the 3-A Sanitary Standards committee that quickly recognized the need for standards and practices to guide the application of the developing technology.

As the biopharmaceutical industry became clean-in-place users, the major application was to new projects. Most of the manufacturing companies lacked architects, engineers, and construction managers, and the overall design responsibility was necessarily delegated to large engineering companies. The selected firm often determined how clean-in-place would be applied, developing voluminous documentation describing its design, fabrication, and operation. Each new project was treated as a unique, different, and demanding application. During this same

period, the industry recognized the need for "validatable cleaning" and clean-in-place was quickly recognized as a useful tool in meeting that need. The validation requirements for biopharmaceutical processes quickly spread to include all components of the clean-in-place system, and this has exacerbated the cost and complexity of clean-in-place in today's industry.

Clean-in-place technology is a powerful cleaning process when applied to a well-engineered "CIPable" process, and properly controlled and monitored to achieve the required combination of time, temperature, and concentration for the specific circuit and soil load encountered. The desired results are best assured by a combination of engineering design and end point control. A focus on program performance alone rather than the intricate details of how that program is made to occur has been demonstrated to be effective in dairy, food, and beverage applications for four decades. A change in the criteria for assuring validated cleaning—to apply what is necessary, rather than what is possible—could have great impact on the cost of the hardware and software required.

Dale A. Seiberling

Acknowledgments

During the final years of our life together, my first wife Jean often suggested that I give up the excitement of travel, new projects, and new problems and stay at home and write a book. She supported and encouraged my second love through fifty-four years of continuous activity in a variety of industries. Her ability and willingness to manage the family and home, combined with my use of personal aircraft for expedited travel, enabled my active participation in many phases of the development and commercialization of a technology that has fascinated me since I first wrote a term paper on the subject in 1949. I dedicate this book to Jean F. Seiberling. I also want to thank Informa Healthcare for the opportunity to share a lifetime of wonderfully satisfying experiences. My life's work has touched all peoples in the developed nations of the world in a manner they will never know, let alone comprehend. It is a privilege to help expand the successful application of clean-in-place to biopharmaceutical processes.

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