"There are no days in life so memorable as those which vibrate to some stroke of the imagination."

Ralph Waldo Emerson

Acknowledgement

We would like to thank the editors for their continued guidance and for allowing NPS Pharmaceuticals the opportunity to express our gratitude to those who have helped us achieve our success.

NPS has embarked on an ambitious journey to better the lives of those around us. We realize that our success is the result of the contributions of the researchers who have gone before and those who help us today. We are honored that you have chosen to join us in this endeavor and thank you for helping us bring to fruition the ideas born in our imagination.

The development of new drugs is a challenge that cannot be accomplished alone and your contributions are reflected in our success. Therefore, it is with our sincerest gratitude that we present you with this book. We hope the knowledge contained within will assist you in your endeavors to follow your imagination.

BETTER MEDICINES,
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Derek Pearson and Colin G. Miller (Eds)

Clinical Trials in Osteoporosis

With 48 Figures

Springer

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Cover illustration: Lateral X-ray film of the Lumbar vertebrae shown in a "Hot Iron" colour scheme. Image reproduced by courtesy of Bio-Imaging Technologies Inc.

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Foreword

by Ignac Fogelman

Prior to the mid 1990s, very few people were aware of the disease of osteoporosis, not only in the general population, but also in the medical profession. In the last ten years there have been many advances and developments in the understanding of this crippling disease, to the point that this therapeutic field has lost its "fledgling" status and has grown up rapidly. This is well demonstrated by the number of effective therapies that are available, the new methodologies for the diagnosis and monitoring of the disease and the fact that the importance of osteoporosis, as a disease, is now recognized and is taught as an integral part of the syllabus in most medical schools.

With the maturation of this therapeutic area, it has now become a challenge for physicians, scientists and technologists to gain an easy understanding of the intricacies of running studies or clinical trials in osteoporosis. This book provides an excellent introduction and handbook for those wishing to pursue research in this field. It not only provides an overview of the field of osteoporosis, the measurement methodologies available and current therapies, but also covers all the necessary regulations and Good Clinical Practice (GCP) requirements that are both specific to the disease state, and generic across all clinical trials. Furthermore, an interesting slant has been taken in providing "mock trial data". The reader is then taken through the analysis of the study and rather than having to do this theoretically, can work with the data provided. It will then be very straightforward for the reader to apply the calculations derived to their own data.

This book has been written in an easy-to-read style, and novices to the field of osteoporosis and/or clinical trials will be guided through the whole process. It is unusual on two major accounts; firstly it has been written to appeal to those working in the pharmaceutical industry, as well as those at the trial site: principal investigators, study site coordinators and bone densitometry technologists. This has been achieved by the inclusion of several guest chapters, so the whole clinical trial arena has been covered. Secondly, this book has been written with both the European and American markets in mind. The principal authors, while both British, live on opposite sides of the Atlantic, and so the book has a very comprehensive feel to it. This unusual meld of editors and authors, from both industry and

academia, has provided a unique opportunity for the development of this book, encompassing the many facets of clinical trials in osteoporosis. The addition of several notable guest authors has increased the depth of this book.

As a physician who has been involved in the field of osteoporosis for many years, I believe that this book enters the marketplace in a timely manner. Since the field has matured, this reference work is needed to help the researcher obtain the principles of the disease and clinical trial environment in a rapid and convenient manner. It answers most of the basic questions, and many of the more complex ones. Since it covers the clinical trial start-up, right through to data analysis and publication, it will become a very useful and widely used handbook. While some will read it from beginning to end it also lends itself to being dipped into at the appropriate points in a trial life-cycle, without having to be onerous on time, which is rarely available in great quantities to anyone involved in clinical trials.

Ignac Fogelman
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Contributor Biographies

Dorothy Adams is an experienced Research Administrator, having been involved in the running of numerous osteoporosis trials. She is an Executive Director of the Jackson Foundation, a clinical research organization based in Madison, Wisconsin.

Penny Blackwell graduated from Birmingham University in Biochemistry and trained in Clinical Biochemistry at Nottingham City Hospital. She obtained her PhD in bone biochemistry in 2000, and is now a third year medical student. She plays the French horn particularly well.

Sue Cawte is currently employed as a Superintendent Radiographer responsible for the bone densitometry service at Nottingham City Hospital. She has worked in this field for over nine years, being involved with clinical patients and over 40 bone densitometry research trials. During this time the development of the capability of DXA machines to perform MXA led to her pursuing and gaining an MPhil in spinal morphometry. She is currently developing a radiographer reporting service. She has strong links with the University of Derby distance learning program, writing about the practical aspects of DXA for the osteoporosis modules. She is also a module tutor.

Ian Godber is a graduate of the Universities of St Andrews and Dundee. Ian trained as a Clinical Biochemist at Ninewells Hospital in Dundee, during which time he completed an MSc at the University of Surrey. He took up his current position as a Senior Clinical Biochemist at Nottingham City Hospital in January 2000. His main responsibilities include coordinating the biochemical analyses involved in a number of research projects. His main areas of interest include biochemical markers of bone turnover and calcium homeostasis, GC-MS analysis of both drugs of abuse and organic acids. He also maintains the Association of Clinical Biochemists website.

David Hosking is a Consultant Physician and Professor of Mineral Metabolism at Nottingham City Hospital. After postgraduate training in Birmingham he went to the University of Leiden as an MRC Travelling Fellow to work in the Department of Endocrinology. His research interests are in the fields of osteoporosis, Paget's disease and

vitamin D metabolism. He has published over a hundred papers in this field and is co-author of a textbook on the *Management of Metabolic Bone Disease.*

Nigel Lawson graduated from the Biochemistry Department at the University of Sheffield in 1976, and obtained his PhD on the control of lipid synthesis from the University of Nottingham in 1980. After undertaking, some more research in lipids he worked in the Clinical Chemistry Departments of East Birmingham Hospital and the Birmingham Children's Hospital, plus the Regional Immunology Department in Birmingham. Nigel moved to the Clinical Chemistry Department at the City Hospital in 1991 to take up the post of Consultant Clinical Scientist and was made a Fellow of the Royal College of Pathologists in 1997.

Colin Miller graduated in 1983 from the University of Sheffield with a degree in Physiology and Zoology. He worked for four years as a Research Assistant at Bio-Engineering Research Unit, Doncaster University and then as a Clinical Research Associate (CRA), Syntex Research, Department of Clinical Pharmacology and Therapeutics Investigation. During this time he obtained a PhD from Hull University, on The Measurement of Broadband Ultrasonic Attenuation (BUA) for Assessing Hip Fracture in the Elderly. Since then he has worked as a Clinical Research Coordinator, Norwich Eaton Limited (a Procter & Gamble Company) and as Head of the Physical Measurements Team, Europe, Procter & Gamble Pharmaceuticals. Between 1991 and 1993 he worked on a part-time basis at Guys Hospital in the Department of Nuclear Medicine working for Dr Ignac Fogelman. From 1994 he was Director of Clinical Services, Bona Fide Ltd (a wholly owned subsidiary of the Lunar Corporation), taking up his current post as Vice President, Business Development, Bio-Imaging Technologies Inc. in 1999. He has been a reviewer for *Osteoporosis International*, the *Journal of Clinical Densitometry*, the *British Journal of Clinical Research*, the *European Journal of Clinical Research* and, most recently, the *Journal of Clinical Research.*

Derek Pearson graduated in Physics from Nottingham University in 1976. He obtained a PhD in Medical Physics from the University of Surrey and then spent three years as a post-doctoral fellow at the University of Leeds working in the Body Composition group. He moved back to Nottingham in 1982 to work as a senior grade physicist in Nuclear Medicine. He has been Clinical Director of Medical Physics at Nottingham City Hospital NHS Trust since 1989. He has a broad range of interests in imaging and radiation physics and has published over 30 papers, most recently specializing in the measurement of bone density and tele-medicine.

David Reid is an honorary consultant rheumatologist and Professor of Rheumatology at the University of Aberdeen. He has research interests in bone mass assessment, corticosteroid induced osteoporosis, cost-

effectiveness of screening for osteoporosis, clinical outcome assessment in rheumatoid arthritis and osteoporosis, clinical trials in osteoporosis and arthritis. He is Treasurer and Scientific Advisory Committee member for the National Osteoporosis Society, a Member of the Scientific Organizing Committees for the International Bath Conference on Osteoporosis 2001, and the European League and Against Rheumatism Congress, Glasgow 1999.