



NEW RAPID FDA STRATEGY QUESTION AND ANSWER SERVICE

SAGE'S NEW RAPID FDA STRATEGY Q&A SERVICE

History tells us that FDA has rejected many more products than it has approved. Answering FDA strategy questions is critical to successful product development. Although there may be several potential approaches to obtaining FDA approval for your product, not all of these approaches will result in FDA approval. Some approaches that may eventually lead to FDA approval also may not be time and resource effective. We have often found that companies have a limited number of important questions, the answers to which can guide them toward the most effective product development strategy. Sage can answer these questions quickly and provide a more detailed response as well. Through the convenience and speed of modern communications technology, your regulatory strategy questions can be answered in a timely, effective and inexpensive manner.

The Sage Group is able to provide answers to your product specific FDA regulatory strategy questions, answers that will be directed at identifying successful FDA product approval strategies. The answers will be provided to you by Sage's Senior Advisor, Peter Levitch and his associates, and will be based upon years of successful experience in developing FDA regulatory strategies that have led to FDA approvals of a number of products. In addition, the answers will take into consideration FDA regulations and requirements of today. Mr. Levitch and his associates have helped a diverse group of companies achieve FDA product approvals. These companies include large pharmaceutical companies, and start-up companies and the products encompass new molecular entities, biologics, medical devices and *in vitro* diagnostics. This service will enable you to eliminate the cost, formality and the time of engaging full time or part time regulatory affairs experts. This service will result in potentially speeding up *your* path to FDA product approval. Save time, resources and above all else, avoid false starts, by utilizing the experience and success of Peter Levitch and his associates to answer your FDA regulatory strategy questions, all for a firm quotation provided before the work begins. Fees will be reasonable, starting at as little as \$1,000 and range upward depending upon the complexity of the question and answer. Confidentiality is assured, and can be formalized to suit your needs.

EXAMPLES OF REGULATORY STRATEGY QUESTIONS WE CAN ANSWER QUICKLY

- My company has a product for a specific indication. We are in a rush to move this product forward quickly. Is it necessary that we conduct our first clinical study in healthy, male volunteers, as this seems a waste of time and resources?
- My company has a product which has a unique formulation for an indication at which no other company is looking. Which part of FDA has jurisdiction over our new product?
- FDA has placed our IND product on clinical hold. What can we do to expedite getting removing clinical hold and getting our studies underway?
- My company's product is indicated for a small patient population. Is there any real advantage to obtaining orphan drug status?
- My company has a drug product in Phase 3 studies. Our manufacturing group has determined a new, faster, cheaper way to manufacture this product. Can we use this new process to make product to complete our Phase 3 studies?
- Is it necessary to complete stability studies prior to starting our planned Phase 1 clinical trial?
- Do pharmacology studies in animal models for efficacy have to be conducted under Good Laboratory Practices Requirements?



- An advisor to my company suggested that we do drug distribution studies in animals. Would it be of any value to radiolabel our product, administer it to animals and trace distribution of the radiolabel?
- My company management thinks it wishes to meet with FDA to help plan the clinical development of our product. In general, can an FDA meeting be useful? How can my company schedule an FDA meeting? Are there any down-side risks to having such a meeting? How should we position such a meeting? Who from our sponsor's team attend such a meeting? Can we request specific FDA staff members to also attend this meeting?
- Is it possible to conduct any clinical study without first filing an IND/IDE? Is it possible to conduct any clinical study without obtaining Institutional Review Board (IRB) approval?
- My company is developing a product for a specific indication. We learned that FDA has a guideline for products for this specific indication. However, upon review of this guideline, we realize we cannot apply the guideline to our product. Is there anything we can do, or are we totally blocked from going forward?
- My company has a totally unique, one of a kind formulation. In trying to complete Item 7 Chemistry, Manufacture and Controls (CMC) we are not able to fully characterize our product due to its unique formulation. Is there a way for us to proceed with our IND without fully characterizing our product?
- Is it an FDA requirement that we identify the lowest effective dose of our product, and conduct studies to prove its efficacy at that dose?
- How can my company gain advantage using FDA's position regarding surrogate markers?
- My company has a product which is expensive to manufacture. Can we recover any of these manufacturing costs from investigators or patients during our clinical studies? Is it generally a good idea that we try to recover costs?
- My company wishes to conduct some of its clinical trials in Europe or Asia. Does FDA accept non-US generated clinical data? If FDA does accept non-US generated data, are there any provisos we should be aware of?
- I have heard the term potency and specific activity used. Should my company be thinking about ways to measure the potency or specific activity of our product?
- I have heard the term: Treatment IND. What is it, and is it something I should be planning on using during my product development?
- One of the products my company is developing seems to have potential clinical benefit for several different, unrelated indications. Should we pursue them all, or if not, how should we select the one indication we should start studying?
- My company is developing a drug, but at this early stage of development, we do not know what the dose, or course of therapy might be. How do we design toxicity studies which will allow us to proceed into human studies?
- I have learned that some clinical studies weren't correctly powered. What does correctly powered mean, and how to I assure that my future study will be correctly powered?
- What does a favorable benefit-to-risk ratio mean? What does a favorable therapeutic index mean?
- What are some of the reasons for FDA not approving a product?
- What product specifications are important?
- Is it possible for my company to use an outside laboratory to conduct quality control (QC) studies?
- Is there a difference between quality control (QC) and quality assurance (QA)? If there is a difference, does my company need both of these?
- A contract manufacturer told my company that it is FDA approved; therefore my company can have the contract manufacturer produce its product in compliance with GMP. Is this correct?
- What are pharmacokinetic (PK) studies and pharmacodynamic (PD) studies? Should I plan for the need to conduct these during product development?
- What are the different phases of clinical studies? What approximate number of patients do I need to plan on for each phase of study? May I start Phase 3 prior to completing Phase 2?



GETTING ANSWERS TO YOUR FDA REGULATORY STRATEGY QUESTIONS

When you have selected and/or formulated an FDA regulatory strategy question, you should contact Sage by email at TheSageGroup3@aol.com, indicating convenient times for a short telephone call. Peter Levitch will call you to obtain details of your question and provide you with a firm cost quotation. He will then conduct the necessary research to develop an answer in keeping with current FDA requirements. He will then formulate the answer and call you with the result before providing the answer in writing. Although it is anticipated that all questions will require some amount of research and thought to answer, the writing of each answer will be carefully accomplished to ensure a complete, unambiguous answer which will have value to the questioner. If a question is complex, therefore requiring a complex in-depth answer, the questioner has the option to have an in-depth discussion with Peter for the purpose of formulating a complete answer. Additionally, if further discussion is desired after receipt of an answer, such discussion can be arranged. This service may be useful as a first-line strategy development, to provide a second opinion on a strategy, or to formulate a new strategy when your original strategy has encountered an FDA hurdle or rejection.

PETER LEVITCH

Peter Levitch, BA, MA has provided informed guidance in the development of pharmaceuticals, medical devices, biologics, and diagnostics for more than 30 years with a strong emphasis on biotechnology derived products through the clinical evaluation and FDA regulatory approval phases of product development.

Peter's expertise encompasses:

- Strategic Regulatory Planning for Product Development leading to FDA regulatory approval
- GMP Audits and Inspections
- Preparation/Review of Submissions to FDA
- Clinical Research Study Design aimed at generating data for FDA approvable indications
- Conduct of In-House Training Programs in Clinical Research (Study Design) and Good Clinical Practices, Regulatory Affairs and Preparing for FDA Inspections
- Schedule, Establish Agenda, Conduct Rehearsals for, and Attend (often as host) FDA/Company Meetings
- FDA Liaison
- Consulting in Regulatory Affairs and Clinical Research on an as needed basis
- Clients include biotechnology companies (some from initial startup to profitable position) pharmaceutical companies, medical device companies, diagnostic product companies, investment bankers and venture capital funds.

Peter's accomplishments include:

- Consulted to more than 200 pharmaceutical and biotechnology companies, including Amgen, Genentech, DuPont, Monsanto, J&J, Coulter, Chiron, Grace, Kodak, Oncogene Sciences, Interferon Sciences, Lilly, Diamond Shamrock, Kabi, Boots-Celltech, Genetics Institute, Purdue Frederick, Serono.
- Participated in the preparation of more than 260 successful INDs/IDEs.
- Developed successful Strategic Regulatory Plans to guide companies through pathway to FDA approval.
- Participated in the FDA approval of more than 12 biotech products, including erythropoietin, growth/colony stimulating factors, three forms of interferon, Fludarabine, monoclonal antibodies for therapy, imaging and *in vitro* diagnostics.



ENDORSEMENTS

"I was deeply impressed by Peter's knowledge and understanding of FDA requirements as well as his ability to successfully strategize in the context of product development. Furthermore, his innovation regarding clinical design and understanding clinical design in the context of regulatory approval was especially impressive. His clear understanding of FDA needs, perspectives and requirements in such interactions was invaluable.

Paul G. Richardson, M.D., Associate Professor of Medicine, Harvard Medical School

"Peter's strength has always been to lead the way toward achieving the most direct yet comprehensive pathway to an FDA approval."

Patricia W. Bradstreet, President, Bradstreet Clinical Research Associates, Inc.

"Peter is an outstanding regulatory expert. He has intimate knowledge of the FDA and its requirements across multiple divisions. I have found his insight and acumen in regulatory matters to be of the highest caliber."

Mark J. Pykett, VMD, Ph.D., MBA, President and COO. Alseres Pharmaceuticals Inc.

"Peter was and is a highly knowledgeable expert in U.S. drug development; he also was an energetic worker who was not reticent about rolling up his sleeves and getting actively involved in meeting company goals. He was a lifesaver for me as we worked together to attain marketing approval for a product that has literally changed hundreds of thousands of patients' lives for the better."

Larry Johnson, Consultant in Regulatory Affairs, Formerly Regulatory Director and Responsible Head, Amgen, Inc.,

"Peter is very knowledgeable of FDA IND and pre-marketing requirements and is well suited to assist companies in developing appropriate regulatory strategies to move products through the FDA approval process."

Don Hill, President, Don Hill & Associates, Inc., former Director of Licensing, CBER/FDA

"Peter helped guide us through the regulatory pathway at CBER with both our establishment and product license applications and was instrumental in helping us prepare for our FDA pre-approval inspection and FDA advisory panel meeting. Peter's knowledge has always helped to assure our compliance with FDA requirements.

Dr. Stanley Schutzbank, formerly President, Interferon Sciences, Inc.

THE SAGE GROUP

Sage is a senior-level health care, technology oriented, strategy and transaction advisory firm formed in 1994. The principals of Sage are seven highly experienced healthcare executives, each of whom has substantial strategic, analytical, and hands-on operating experience as well as extensive backgrounds in licensing (in and out), corporate partnering, and M&A. In addition, Sage's Advisors and Senior Directors have extensive knowledge in the clinical, regulatory and product development disciplines. Sage's principals have played key leadership roles as founders/CEOs/senior managers in a number of emerging biomedical companies. They have also played key consulting roles in corporate partnering/acquisition and licensing strategies of emerging and mid-sized companies.

The Sage Group has extensive, hands-on operating and consulting experience in small, medium and large companies active in:

- Pharmaceuticals
- Biotechnology
- Nutraceuticals
- Life Sciences
- Drug Discovery
- Medical Devices
- Drug Delivery
- Diagnostics
- Animal Health
- Generic Drugs
- Analytical Instrumentation

The Sage Group Principals



- Wayne Pambianchi, has been actively involved in strategic analyses and transactions for over 25 years and has completed numerous mergers, acquisitions and divestitures, internationally. He has worked extensively with bioanalytical companies globally.
- Yoshihiro Mizuta runs Sage Group Japan, Inc. and has held senior positions in the Japanese pharmaceutical industry as well as serving in significant advisory roles, which makes him extremely well networked in the Japanese pharmaceutical marketplace.
- Dr. Dan Tripodi has a Ph.D. in immunology and has engaged in a number of licensing, business development, and alliance programs (mostly to bring products in) while working with Johnson & Johnson in senior marketing, technology and strategic planning for more than 20 years.
- Dr. William Mason runs Sage's European office and is very well networked in the European pharmaceutical and bioanalytical industry. Dr. Mason also has considerable experience in mergers, acquisitions, licensing and alliances that both bring in and out-place products and technologies in Europe and ROW. His academic background is at PhD level in bioanalytical instrumentation and molecular biology.
- Gordon Ramseier was responsible for introducing the so-called "Dura Strategy" while he was CEO of Immunetech Pharmaceuticals, the precursor to Dura Pharmaceuticals. During his tenure of involvement at Dura, the company in-licensed and acquired a large number of products.
- R. Douglas Hulse was Vice President of Business Development at Enzon, Inc., one of the leading companies in protein replacement therapy. In this capacity he led a program of more than 30 licensing deals and an acquisition.
- Charles Casamento, has held a number of marketing, sales, finance and business development positions with Sandoz, Hoffmann-LaRoche, Johnson & Johnson and American Hospital Supply Corporation where he was Vice President of Business Development and Strategic Planning for the Critical Care Division.



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