



Biopharmaceutical Report

Chair: *Tom Capizzi*

Editors: *Demissie Alemayehu, Kannan Natarajan, and Ersen Arseven*

Editor's Note

Demissie Alemayehu

As promised, the current issue of the Biopharmaceutical Report features a paper on the role of statisticians in post-approval drug development. The authors, who have considerable experience in the area, give a valuable perspective that will certainly help raise awareness about the contribution of statisticians in the later stages of drug development.

Continuing its fine tradition, the Biopharmaceutical Report will feature high quality papers of particular interest to the biopharmaceutical community in future issues. It is recognized that there is a growing demand for reprints of past featured articles, as evidenced by the numerous requests the office of the American Statistical Association and the editors have received. To this effect, an effort is being made to make past issues accessible online, via the Biopharmaceutical Web site (www.best.com/~asabp). In this regard, we'd like to acknowledge the significant contribution of our Webmaster, Kalyan Ghosh of Merck Research Laboratories.

Challenges and Opportunities of Biometrics in Post-Approval Drug Development

Ed Whalen, Ph.D.

and

Marcia Levenstein, Sc.D.,

Ed Whalen is Director, and Marcia Levenstein is Senior Director/Group Leader, Biometrics Department, Clinical Data Operation, Pfizer Inc., New York, NY 10017

Abstract

The biometric components of a drug's development carry on well past the submission to regulators for approval to market the drug. However, the level of biometrics involvement in the post-approval environment has typically been limited to supporting Phase IV trials. The analytical content can be quite extensive in many of the other post-approval activities. Biometrics, in

Contents

Editor's Note

.....ALEMAYEHU 1

FEATURED ARTICLE

Challenges and Opportunities of Biometrics in Post-Approval Drug Development

.....WHALEN & LEVENSTEIN 1

Letter from the Chair

.....CAPIZZI 8

Looking Ahead to 2001

.....MEEKER 10

BIOPHARMACEUTICAL SECTION NEWS

Summary of Minutes Of ASA Biopharmaceutical Section

.....CAPIZZI 10

ENAR 2001 Spring Meeting

.....HEFT 11

Annual FDA/Industry Workshop: Statistically Sound Decision Making

.....CAMPBELL & HEFT 11

ASA Fellows Update

.....DAVIS & GOULD 12

56th Deming Conference 12

24th Annual Midwest Biopharmaceutical Statistics Workshop 13

Biopharmaceutical Section Functions (2000) 14

general, and statisticians, specifically, need to seize the opportunity to strengthen the scientific and commercial value of that analytical content.

1 Introduction

The role of biometrics must broaden to include collaboration with pharmaceutical marketers, clinicians, regulatory personnel, and outcomes researchers. Commitment to satisfying their analytical and analytically based business needs raises the opportunity to provide a clearer analytical perspective to them and their audiences (e.g., physicians, patients, reimbursement authorities, and regulatory bodies). It also broadens the scope of a statistician's work and strengthens the efforts of these stakeholders.

A pharmaceutical product's development process spans drug discovery in the lab to production and marketing of generics following the loss of patent protection. Statisticians have typically played a significant role during planning and conduct of studies aimed at submission of the drug for regulatory approval (Phase I through III studies). In recent years there has been growing involvement by statisticians in post-approval development. However the dominant paradigm still seems to be oriented toward statisticians functioning as clinical trial statisticians—in this case for Phase IV clinical trials. Challenges and opportunities for pharmaceutical statisticians reside in breaking from this paradigm and venturing into other areas where analytical expertise can add value to the pharmaceutical product and ultimately lead to benefits for patients.

The first step in expanding the efforts of statisticians is to understand the needs of the different stakeholders regarding analytically based information. If one looks at any drug advertisement it is likely there are analytically based statements woven into the ad. Making clearer that analytical portion is, in spirit, no different for pharmaceutical statisticians than the type of work exemplified in texts such as Tuft's (1983) classic. The goal is to be understood by the audience affected by the analytical work. The obvious difference between the pre-approval and post-approval duties of the statistician is not in statistical methodology, but in the ultimate audience. Regulatory bodies no longer compose the only audience, though they still are one of the important audiences, in the post-approval environment.

Post-approval development offers new opportunities and the corresponding responsibilities. However, the familiar responsibilities of a clinical trial statistician still remain and must be met. For example, the statistician still needs to ensure the implementation of ICH or FDA guidelines in the context of Phase IV trials, quality of data and analyses, and the use of proper techniques in meta-analyses of study drug data. For clarity, regarding Phase IV studies and other post-approval development of a drug, consider the following from the FDA's website:

Phase IV begins after drug approval. Therapeutic use studies are considered to be those trials that go beyond the prior demonstration of the drug's safety, effectiveness, and dose definition.

Studies in Phase IV are all studies (other than routine surveillance) performed after drug approval and related to

the approved indication. They are not considered necessary for approval but are often important for optimizing the drug's use. They may be of any type but should have valid scientific objectives. Commonly conducted studies include additional drug-drug interaction, dose-response, or safety studies and studies designed to support an extended claim under the approved indication, e.g., mortality/morbidity studies.

Development of an application unrelated to the original approved use should be seen as needing a separate development program, though the need for some studies may be obviated by the availability of data from the original development program.

After initial approval, drug development may require continued study of new or modified indications, new dosage regimens, new routes of administration, or additional patient populations. If a new dose, formulation, or combination is studied, additional human pharmacology studies may be indicated.

Biometrics has a clear role to play so that statements such as ". . . should have valid scientific objectives" are met with the same level of rigor as required in earlier phase studies. Thus for a well run Phase IV study biometrics should become involved and follow the same high standards as in Phases I-III. This reinforces the need to have well planned and documented design, analyses, and reporting methods for Phase IV studies. Furthermore, as suggested by the third paragraph of the above FDA statement, evidence required for gaining other indications may partially be supplied by existing information—perhaps Phase IV studies in a different disease unrelated to those in the drug's approved indications.

Although Phase IV studies stand as a very important part of the post-approval landscape, there is much more. New opportunities, challenges and responsibilities are found in the collaboration and support that is provided to marketers and clinicians in creating promotional pieces as well as deciding on and executing a publication and presentation program. Successful statisticians need to understand the type of broad collaboration required and the additional necessary skills to accomplish this. These are the questions and issues that arise in the less structured environment surrounding post-approval biometrics.

2 The Needs of the Stakeholders

The traditional audience for a statistician's work in Phases I to III is explicitly understood through guidelines such as the ICH and FDA guidelines (e.g. ICH guidelines E2A-E2C and E9). Much of the content of those guidelines is applicable to Phase IV studies. However, in the context of many other post-approval activities the audiences are more diverse and guidelines, if any, are less well documented. Therefore, it is important to understand the various disciplines within the pharmaceutical company and how they work to reach these audiences. It is also important to contemplate developing an appreciation for the needs of these audiences. Both the internal (to the pharmaceutical company) and external players are stakeholders in the process and production of clinical and marketing infor-

mation about a drug. Learning about these stakeholders' interests and needs is critical for putting a useful structure on the statistician's work so that it holds true to the content and inspiration of guidelines such as those developed by the ICH tripartite.

The disciplines involved with a drug's clinical and marketing development shift in emphasis following its regulatory approval for marketing. Responsibilities for the drug's further development moves from submissions experts to marketers, Phase IV/post-approval clinicians and regulatory personnel, and outcomes researchers (e.g., health economists). The people who fulfill these roles may be the same individuals who moved the drug through the submission process or they may be a separate group depending on the structure of the corporation. Nevertheless these are the roles that need to be filled within the pharmaceutical corporation in order to market the drug and develop it further. These stakeholders' analytical concerns reflect and include those of external stakeholders (external to the company) such as reimbursing authorities, regulatory safety reporting units, and promotion regulators such as the FDA's Division of Drug Marketing, Advertising, and Communications (DDMAC).

The external stakeholders are many, given the global nature of today's pharmaceutical companies and markets. Because each country has its own rules regarding what is allowed in advertisements, it is not possible to go into the details here. However, a look at the mandate for DDMAC can be helpful in getting a sense of what some of the issues are and how they may affect the interests and needs of various stakeholders—specifically those within the company. DDMAC's mission is "to protect the public health by assuring prescription drug information is truthful, balanced, and accurately communicated. This is accomplished through a comprehensive surveillance, enforcement and education program, and by fostering better communication of labeling and promotional information to both health professionals and consumers." (<http://www.fda.gov/cder/ddmac/>).

A marketer is concerned with the regulatory worthiness of any piece related to the drug's promotion as part of general marketing ethics, see e.g., Cateora and Graham (1999). As DDMAC's mission statement makes clear, regulators pay attention to how the company promotes its product. The requirement for "truthful, balanced, and accurately communicated" information implies, among other things, analytical accuracy. This need not be viewed merely as a restrictive burden of proof, but can also form an opportunity to help prove the drug's value. Although a given statement's accuracy may be based on a clinical report or other such document, stronger statements may be attainable if the statistician has an appreciation for what the marketer is trying to accomplish. By doing so, it opens the door to consider further analyses so long as they are valid statistically and scientifically and, hence, valid in the eyes of authorities such as DDMAC.

Company personnel have a responsibility to ensure that the company lives up to the requirements implied in DDMAC's mission statement. Thoughtful and timely statistical advice are needed to ensure that the contents of drug

promotional pieces are sound from a statistical point of view (design, analysis, etc). Here too, participation by the statistician can provide comfort to the company that a given marketing piece will stand up to regulatory scrutiny or, if not, then provide insights regarding the limitations of the piece.

Statisticians have inherent reasons to care about these stakeholders, because, along with the other disciplines, biometrics is significant part of the post-approval drug development process. For example, in a well run Phase IV clinical study, the role of biometrics is not distinguishable from its role in a submission study. Thus biometrics' commitment to the trial should model that from earlier phase studies. Furthermore, biometrics involvement in Phase IV can act as a springboard from which to access other stakeholder activities, determine the analytical needs, and provide insight to how biometrics can help meet them.

Beyond statisticians supporting clinicians running Phase IV studies and providing regulatory safety updates, a marketer may need timely information to respond to a change in the marketplace. The particulars of the analysis may require obtaining information from several data sources and collaborating with clinicians, marketers, and company regulatory advisors to create a response piece that will meet the market need and satisfy the regulatory scrutiny of the country where the piece is to be used. The statistical and data management techniques available to formulate such a response can cover the spectrum from use of clinical trial data to information in the public domain such as references in the clinical and outcomes literature or meta-analyses of studies or literature.

The requirement for clinical information to support reimbursement decisions, and perhaps to obtain overall approval, has become very common. Reimbursement authorities in a country, province, or region may require additional information to approve the drug for formulary reimbursement. The role of the statistician to evaluate information from multiple sources, provides the environment for collaboration among clinical, marketing, regulatory, statistical, and outcomes personnel. The need is evident as influential bodies such as the UK's National Institute for Clinical Excellence (NICE) continue to grow in importance. An example of this type of challenge to a drug's market potential is covered in the Wall Street Journal (November 22, 2000). In these situations the required response is not formed in a vacuum by one or two disciplines but results from a concerted effort utilizing the talents of many disciplines (including biometrics) across several countries. Such examples show that the market and regulatory environments for pharmaceuticals have evolved to the point where there is need to respond to analytically based questions which can come from virtually anywhere.

Potential Areas for Increasing Biometrics Involvement

The disciplines and institutions discussed in the last section may be involved in or affect various post-approval development activities. One obvious area to consider is the product's launch preparation. Drug launch is the first time

in the drug's development that promotional pieces and messages will appear. At most companies, it is a critical step in the drug's market life. Much of the Phase III and prior information will be presented, as will Phase IV results if they are available. The post-approval statistician may not have worked on any of these studies but may play a critical role for ensuring that any analytical information is correct in content, method, and final presentation (e.g., visual aids used in the drug's promotion).

The various informational pieces (especially promotional visual aids) created for the product's launch will likely need to be updated throughout the drug's life cycle. New information from post-approval studies and meta-analyses of existing studies may find placement in the various visual aids given to the company's promotional representatives for their use in promoting the drug. The process by which a company creates the promotional pieces varies across the pharmaceutical industry but the end result is similar to what is seen in print and television advertisements for drugs. The analytical content of these items varies depending on the audience (advertisements being substantially different from a visual aid used by a company representative promoting the drug in a physician's office). Nevertheless the company's processes for creating these pieces offer opportunities for statisticians to work with the other stakeholders (marketers, clinicians, outcomes researchers, and regulatory advisors) to create materials that are analytically defensible, meaningful to the target audience, and easily understood without diluting their power. The statistician can make a meaningful contribution by gaining a clear understanding of the needs and then actively participating in the processes. The challenge here is similar to that for the other areas discussed in that biometrics has to find ways to gain access to these stakeholders and processes while remaining within the bounds of the company's culture. However the rewards for the company, scientific community, physicians, patients, and biometrics may well be worth the effort.

Marketers and clinicians spend considerable time and effort in creating the messages and promotional visual aids that are used when presenting the drug to physicians. In this situation the company representatives are affected by the level of biometrics' involvement in the sense that the representatives will need to relearn information if the promotional visual aid contains unsatisfactory statistical information. They are also affected in the sense that they deserve to have the most useful yet easily explained presentation of any analytical information. Early input by a statistician can be very helpful if done with sensitivity to the pressures faced by company staff working in the field markets. The typical time available to promote to a physician is a precious few minutes. In those few minutes the value of a drug needs to be effectively communicated when, for example, promoting to a physician in the U.S. pharmaceutical market. Issues regarding time and content also apply to other audiences such as reimbursement authorities (both public and private such as HMO's). Even though more time and contact may be allowed, marketers and outcomes personnel presenting information to such groups will likely need

to cover more information and with a more visible level of analytical detail. The particulars of such presentations and the corresponding analytical work will vary depending on the country, region, and market. Thus it is important to get involved early with the creation of promotional and related materials.

Product label information (the package insert) is another area in which biometrics' role and active participation is critical. The ability to maximize the drug's value hinges on the strength of its label. Product labels are updated throughout a drug's life cycle. The post-approval statistician needs to be familiar with relevant studies and/or analyses that are involved in any label enhancements. Thus the role played by a statistician should not be appreciably different from what it is for the original submission (e.g., NDA). A natural extension regards submissions for approval of the drug for new uses (e.g., a Supplemental New Drug Application (sNDA)). These submissions are intended to expand the drug's market reach as well as respond to clinical needs and market dynamics. It is expected that they will enhance or extend the product's life cycle. Thus, given their considerable analytical content, biometrics involvement is necessary in supplemental submissions specifically and label related activities in general.

A third major part of post-approval drug development is the publication and presentation of clinical and scientific information. The publication strategy may be expansive or narrowly focussed, but all manuscripts prepared for peer-reviewed journals will be subjected to reviewers who expect analytical rigor. A statistician who becomes part of the publication creation process has the opportunity to further develop analyses from an original study report. The motivation for further analyses may come from the authors, a reviewer, or grow out of dialogue between the statistician and others involved with creating the manuscript. Without participating in the process it is unlikely that the statistician will see any analytical opportunities to strengthen a manuscript. The same can be said for producing presentations for scientific meetings.

Once the drug is on the market, practicing physicians may have questions that the company's promotional representatives may not be able to answer. In these instances the representative informs the physician to call the company directly and obtain information from company clinical staff. This is an example of medical-to-medical communications. Materials for medical-to-medical communications will likely be derived from the company's wealth of clinical information on the drug—as opposed to directing the physician to published literature. The format and content of that information may at times require analytical input from the statistician. Even though some of the information may come from a medical report, it will be condensed into a format that can easily be distributed to the inquiring physician. Therefore, the statistician can provide invaluable help to company medical staff in distilling the information as needed.

Product defense is a somewhat different area from the others and one in which biometrics is usually involved. Taking a more active role may be appropriate depending on

the company and its post-approval biometrics group structure. Much is gained from having the necessary resources in place before the company is called upon to defend the drug's safety. The rash of recent drug recalls magnifies the need for a company to have a mechanism in place for addressing any concerns regarding safety. It also helps the company to understand the concerns of regulators when trying to determine the best solution if there is a well-founded safety issue. Well organized, comprehensive data repositories are an obvious part of the solution.

Post-marketing surveillance feeds into the issues associated with product defense. The decisions surrounding inclusion of spontaneous report data in a product defense are not simple. A statistician's input is critical for aiding in these decisions. Pharmacoepidemiology intertwines with post-marketing surveillance and represents an area in which statistical expertise fits naturally. The potential need for biometrics' involvement is suggested in statements such as the following from the FDA website (<http://www.fda.gov/cder/handbook/epidemio.htm>): "... epidemiologists are involved in the design and critique of Phase IV protocols for safety studies performed by industry, and in the review of study findings."

3 The Importance of Effective Communications

Communication is often stated as a critical factor in many business settings. "Better communications" are often held out as a panacea for more fundamental problems. This unfortunate overuse of the word communications does not alleviate the need for it in the post-approval setting. To the contrary, communications and a serious look at establishing and improving communications are vital in the multidisciplinary and rapidly changing post-approval environment.

Commitment to developing and maintaining effective communications is a key capability for making sense out of rapidly evolving and unpredictable circumstances such as the current pharmaceuticals market. Other important qualities for dealing with the post-approval environment are described eloquently for businesses in general in Weick (1996). Part of the essence of that paper is that in changing and unpredictable environments it is critical to have constant communications among the various players.

The post-approval environment is one where the statistician may not have the luxury of creating an elaborate set of development plans such as those that might mirror a clinical plan in a submission environment. Instead the marketers, clinicians, outcomes researchers and other stakeholders have to spend significant amounts of time and energy responding to the market and regulatory pressures from outside the company. As indicated by Weick's example, everyone who has an effect on the outcome of such an endeavor needs to be aware of the others engaged in that endeavor.

The purpose of this section is not to provide a tutorial on effective communications but to outline areas where it is worth considering the need for improving communications. The first such area is not new to pharmaceutical sta-

tisticians. The interactions with clinical colleagues can be one of the most rewarding parts of putting together an NDA. These interactions are just as critical if not more so in post-approval biometrics work. The same is true for communications with regulatory personnel within the company. The work of company regulatory staff is substantively different in the post-approval environment (see for example DDMAC's webpage of frequently asked questions at <http://www.fda.gov/cder/ddmac/FAQS.HTM>).

A more challenging communications problem may rest in determining methods for learning about and understanding the responsibilities of marketers. Even if the biometrics group rarely works directly with marketers it is still important to develop an appreciation of their point of view. They are typically individuals who know best what needs to be said using the information developed from clinical data (e.g., studies or meta-analyses). Attendance at meetings led by marketers and involving clinical staff is just one possibility for getting exposure to the marketer's perspective.

The communication needs vary considerably, so it is difficult, but essential, to understand and balance these diverse requirements. The global nature of drug development necessitates that statisticians have access to and gain an understanding of these multiple needs.

4 Data Management and Analytical Considerations

ICH-type guidelines on clinical development plans are inherently strategic and appropriately so because the aim is marketing approval or further development as in sNDAs. The issues addressed in those documents are still valid in the setting that we are discussing despite it being a setting where strategies are revised often. Timely responsiveness is critically important due to market dynamics. Thus methods are needed for achieving traditional and vital goals such as minimizing bias, maximizing precision, and assessing risk/benefit while allowing the flexibility to respond in a timely and defensible fashion.

Post-approval studies, in particular Phase IV studies, have been an area of rapid growth for statisticians' involvement over the past decade. As indicated earlier, the required level of scientific rigor for such studies has risen steadily in the past decade. One such reason is a greater need from pharmaceutical marketers to respond to market challenges with scientifically strong and defensible promotional pieces. A second is greater opportunity and need to increase awareness in the physician community through medical publications and presentations at conferences.

Stakeholders do not always require data from new clinical trials, but rather they need more information. Questions that arise are often answerable by applying an appropriate analytical technique to existing data—either company data or data obtainable from external sources. This involves generation of new information and is a place where the statistical analyst's perspective and expertise can bear valuable fruit for the drug project and consumers. Data are in a sense static (once collected) but new infor-

mation can be generated many times over by applying the right analytical view to the data vis-à-vis the question at hand (clinical, marketing, or otherwise) while maintaining good statistical practices such as analysis plans to guard against data dredging. In this sense the more open environment of post-approval drug marketing provides opportunities for statistical application and creates challenges for making those applications rigorous.

Finally, data capture via the Internet, various new and improved software for data-management, and use of state-of-the-art statistical methods (e.g., multiple imputation techniques, GEE methods, meta-analysis, etc) are some of the tactics for addressing the needs described in Section 2. They are merely means to an end, but they are very important means. The following sections are meant to illustrate some issues regarding these methods in the post-approval context.

Data-Management Related Strides

Timelines in post-approval drug development are not driven by an NDA submission deadline. Rather they are formed out of marketing goals, supplemental submission deadlines, responses to regulatory queries, and publication/presentation deadlines. Information from a study may lose importance if it is not available when the market wants to know the study's results. In situations like these, time is even more critical than in the original submission. Thus all technologies, processes, and talents that can substantially improve on the speed and accuracy of data processing, analysis and reporting are of significant value.

The need to effectively manage data repositories is an important data management responsibility. In addition to individual clinical trial databases many companies keep large data repositories containing consolidated data from the NDA submission as well as post-NDA studies. A statistician's role regarding the use of repositories is often supportive and responsive (e.g. providing analyses in the form of meta-analyses at the request of a regulatory or reimbursement authority). Because the structure and maintenance of these data repositories has a major impact on statisticians' ability to help develop responses, it is essential that statisticians be actively involved in the design and development of the repositories.

The full potential of new technologies such as remote data capture has not been fully realized. These technologies and the corresponding processes for data management and study monitoring can greatly reduce the error and rework in a clinical trial. The problems that these technologies address are speed and quality in developing and utilizing databases. Thereby they can affect cost. Development of the infrastructure and processes to use such new technologies and methods is inevitable and an area where data management can have a very positive impact.

The issues surrounding quality-related problems and their solutions are described in the introductory chapters of Juran and Gryna (1993). It is important to bear them in mind in the context of data processing and analysis. Quality assessment methods have merit regarding the problems of quality and speed found in the context of clinical trials

and their conduct (e.g., as applied to processes for data monitoring at the site and data management in-house). Implementation of quality standard and improvement methodology should be natural for biometrics personnel.

Analytical Considerations

Analysis plans and adherence to pre-defined analysis plans may seem "optional" given the variety of statistical activities and the relative openness in the post-approval development environment. However, creating and adhering to analysis plans is good statistical practice and must be applied in post-approval development as a matter of scientific integrity. Additionally, the biometric integrity of any post-approval activities may come under scrutiny of regulators, editors, or other drug companies. Therefore, it is paramount to create analysis plans while meeting the typically tight timelines in post-approval development. Plans may not be as extensive as in pre-approval work, nevertheless the basic requirements need to be met, for example, various concerns from definition of analysis variables, populations for analysis, and analytical methods to dissemination of results and limits on their interpretation.

Bearing in mind the need for statistically defensible and documented work, statisticians are less constrained in the post-approval environment regarding their choice of analytical techniques. Phase IV studies still need to follow regulatory guidance. However, publications allow for more choice and may even demand use of non-standard analytical methods. A classical example is the use of last-observation-carried-forward (LOCF) approach in the case of repeated measurements over time. This approach may be preferred by certain regulatory bodies but may be considered inappropriate by some medical journals and academics.

Other examples can be found in the FDA guidelines for statistical reporting. These guidelines are established for a broad spectrum of therapies and sponsoring companies. Thus the guidelines may be less than optimal for a specific product or disease state. For this reason it is valuable to search for more powerful (in both the statistical and interpretative senses) analytical methods. An example would be the use of non-standard categorical methods (e.g. multiple imputation or GEE on repeated categorical responses as in Landis and Ten Have (1995)).

Meta-analytic methods constitute a very useful approach to the variety of problems that arise in post-approval development. Examples and general methodology can be found in Petitti (1993), DerSimonian and Laird (1986), Hedges and Olkin (1985), and D'Agostino and Weintraub (1995).

Meta-analysis based on the companies own clinical studies data is a powerful tool for meeting certain clinical information needs of clinicians and marketers. When a large body of data from internal studies does not exist the statistician may have the opportunity to collaborate with clinical, marketing, and/or outcomes colleagues through the application of meta-analytic techniques to studies in the literature. Synthesizing information from a set of similar publications is part of the original inspiration for meta-

analyses. Company statisticians may be in the ideal position to effectively suggest use of these methods in ways not often apparent for addressing the post-approval clinical information needs at pharmaceutical companies. It may provide a useful way to answer some questions of concern without consuming a large amount of resources. For example, assume that another drug on the market makes claims of efficacy based on its best study. If that drug's other efficacy studies are available in the literature then the appropriate meta-analysis may be performed to answer the question regarding that drug's likely true efficacy. Such an analysis may be useful if, for example, there is a compelling need to better understand the other drug's efficacy message (either directly or indirectly) or to provide insight for future clinical work.

Pharmacoepidemiology has grown to the point where it has its own societies and body of literature. The International Society for Pharmacoepidemiology is one such organization complete with its own publications and conferences. O'Neill (1998) provides an overview of methodological considerations. A discussion by Evans (1998) elaborates further on these considerations. An example of some pharmacoepidemiological methods in practice can be found in Reiff-Eldridge et al (2000) where prospective pregnancy registries are used to collect data and estimate risk of birth defects for several drugs.

Interest has grown regarding the use of large but perhaps sparse databases. Examples of such databases are the FDA's database of spontaneous report of serious adverse events or the drug's own clinical studies data repository. The work characterized in DuMouchel (1999) can be useful for querying such databases. The same needs for good statistical practice hold in these contexts. For more on these issues see Friedman and Goldberg (2000).

Meeting the goals of flexibility and responsiveness while maintaining the spirit of ICH-type rigor is one of the important challenges and opportunities in post-approval drug development. Business processes need to support the appropriate designs, plans, and analyses that minimize bias and assure statistical validity. This is consistent with the thrust of ICH and generally good statistical practice. It is also highly valuable in the post-approval context in that it provides a forum for thinking through the clinical and analytical aspects of a marketing question with the appropriate colleagues and gives a basis for defending the results.

5 Responsibilities of the Biometrician

None of the stakeholders discussed in section 2 is required to open a dialogue with biometrics. Instead, pharmaceutical statisticians need to learn about the needs of these individuals in the context of their company and specific project(s). Statisticians who initiate and nurture dialogue with the internal and external consumers of our work can, and need to, learn how the information that we generate is used. Furthermore, direct communication to understand and define the true business needs of the team may provide an opportunity for biometrics to identify the appropriate and relevant analyses that will benefit patients and the scientific community. It would be negligent not to

assess these needs and, if resources are available, act to meet such needs.

As with many business problems the first step in finding solutions starts with establishing good communications. Such communication begins with openness, good listening techniques, and a desire to gain understanding, see Boen and Zahn (1982) and Marquardt (1979). Statisticians are experienced collaborators in many contexts. Post-approval development is in essence a less structured environment in which the statistician is responsible for developing as a collaborator and meaningful contributor.

Finally the statistician has the opportunity and hence the responsibility to drive the analytical aspects of the post-approval development processes. In the biometrics department data management, programming and other functional groups may need to rely on the statistician for guidance regarding what processes and technologies will best help a biometrics department meet the diverse needs of the drug project.

6 Conclusion

The rigor, standards, and guidelines utilized in pre-approval setting need to be met in post-approval environment. The application of ICH and FDA guidelines to Phase IV clinical trials is a natural starting point in the post-approval setting. However, many other post-approval activities also have varying degrees of biometric aspects to them. Incorporating similarly high standards to these activities is one of the challenges for biometrics in the post-approval setting.

Another challenge and opportunity of post-approval development is to address the urgency of market-determined timelines while having methodologically defensible designs and plans for development, implementation, and communication of the required clinical information. Because there is such a wide variety of audiences for such information the statistician needs to understand and be actively involved with multiple disciplines and appreciate their varied needs in the post-approval environment.

The opportunities for biometrics rest in satisfying the challenges presented by post-approval drug development. A key component to understanding and acting on these opportunities is the development of constructive dialogue with the various stakeholders in post-approval drug development. The responsibility for developing and realizing these opportunities starts with biometrics personnel. It needs to be followed by biometrics taking ownership of the information that it generates and following that information to see that it is properly and effectively utilized.

Acknowledgements:

The authors are grateful to Demissie Alemayehu for suggesting the topic and for many constructive comments. The authors would also like to thank the other editors for valuable comments.

References

Boen, J. and Zahn, D.: *The Human Side of Statistical Consulting*, Wadsworth, 1982.

Cateora, P. R., and Graham, J. L.: *International Marketing*, Irwin/McGraw-Hill, 1999.

D'Agostino, R. B., and Weintraub, M.: Meta-analysis: A method for synthesizing research. *Clinical Pharmacology and Therapeutics*, Vol. 58, No. 6., pp. 605-619, 1995.

DuMouchel, W.: Bayesian Data Mining in Large Frequency Tables, With an Application to the FDA Spontaneous Reporting System. *The American Statistician*, Vol. 53, pp. 177-202, 1999.

Evans, S. J. W.: Discussion. *Statistics in Medicine*, Vol. 17, Issues 15-16, pp.1859-1862, 1998.

Hedges, L. and Olkin, I.: *Statistical Methods for Meta-Analysis*, Academic Press, 1985.

Juran, J. M., and Gryna, F. M.: *Quality Planning and Analysis*, McGraw-Hill, 1993.

Marquardt, D. W.: Statistical Consulting in Industry, *The American Statistician*, Vol. 33, pp. 102-107, 1979.

O'Neill, R. T.: Biostatistical considerations in pharmacovigilance and pharmacoepidemiology: linking quantitative risk assessment in pre-market licensure application safety data, post-market alert reports and formal epidemiological studies. *Statistics in Medicine*, Vol. 17, pp.1851-1858, 1998.

Petitti, D. B.: *Meta-Analysis, Decision Analysis, and Cost-Effectiveness Analysis*, Oxford University Press, 1993.

Reiff-Eldridge, R., Heffner, C. R., Ephross, S. A., Tennis, P. S., White, A. D., and Andrews, E. B.: Monitoring pregnancy outcomes after prenatal drug exposure through prospective pregnancy registries: a pharmaceutical company commitment. *American Journal of Obstetrics Gynecology*, pp.159-163, January 2000.

Ten Have, T. R., Landis, J. R., and Weaver, S. L.: Association models for periodontal disease progression: a comparison of methods for clustered binary data. *Statistics in Medicine*, Vol. 14, pp. 413-429, 1995.

Tufte, E. R.: *The Visual Display of Quantitative Information*, Graphics Press, 1983.

Wall Street Journal, UK Watchdog Retracts Relenza Flu-Drug Rebuff, Section B, p. 6, November 22, 2000.

Weick, K.: Prepare Your Organization to Fight Fires, *Harvard Business Review*, May-June 1996.

Letter from the Chair

Tom Capizzi

Merck Research Laboratories

As outgoing chair, this is the last column that Demissie Alemayehu, the editor of this report has asked me to write. As I stated in my first column, the Biopharmaceutical section has a large number of hard working and committed volunteers. It is their involvement that lead to the many accomplishments of the section. The function of the chair is to provide overall guidance and coordination and most importantly not do anything that impedes the efforts of others. This column will highlight some of the major accomplishments and recognize the efforts of our volunteers. I know that I will forget to thank some individuals and misspell the names of some others. I apologize in advance for doing so. I also want to warn readers that much of this column appeared in a January *Amstat News* article.

The section once again had a strong scientific program. Bob Small did a great job putting together the sessions and coordinating the short courses. Having been a program chair myself, I can say that this position is perhaps the most labor intensive one. Thanks to Lukas Makris and Keith Soper for organizing the JSM roundtable topics. Thanks also to all of the session organizers and chairs for their contributions. At the March 2000 ENAR Spring Biometric Society meeting, the section sponsored two invited paper sessions and co-sponsored a theme session. For the 2000 JSM the section did extremely well in the number of invited sessions, special contributed sessions, and regular contributed sessions. We sponsored four invited sessions on a variety of relevant topics: Methods of time to recurrent events analysis, Topics in health economics, Methodological issues in meta-analysis, and What's new in the statistical evaluation of pulmonary drugs. The section also sponsored three topic contributed session and seven regular contributed paper sessions. In addition, we are also sponsored two courses. One was on a classical topic - Equivalence trials: statistical issues —that nonetheless remains vibrant and another on Statistical Methods in Modern Molecular Biology, that is a cutting edge area for biostatisticians. We had 10 luncheon roundtable discussion topics. All sessions, courses, and roundtables were well attended. Keith Soper, as program-chair elect also has organized excellent invited paper sessions for the 2001 JSM.

Our section's business meeting at the JSM was attended by over 150 members. The highlight of the meeting was our awards presentations. There is a considerable amount of effort involved in coordinating these awards. Thanks go to Lukas Makris for working with the ASA office on the administration of these awards. The first authors of 1999 Best contributed paper awards were R.A Railkar (1st place), N. R. Bohidar (2nd place) and L. Helms (3rd place). For the 2000 Best Student Paper Awards, the section increased its efforts in soliciting entries which resulted in nearly twice

as many entries as in 1999. Thanks go to Avital Cnaan (chair), Tom Bradstreet, Sanat Sarkar, and Christine Clark for their planning efforts and their ability to evaluate a large number of manuscripts under tight timelines. Congratulation to the student paper award winners who were J. Bryan, Z. Shang, V. Somayaji, D. Yu, and Q. Yu. I was initially impressed that unlike previous years most of the audience remained after the awards ceremonies. I was about to attribute this to the interesting and lively agenda that I developed until I observed that also unlike previous years there was still plenty of food and refreshments available.

The 2000 Best contributed paper award winners will be announced shortly. I want to thank Doug Faries and Viswanath Devanarayan for their planning and implementation efforts at Indianapolis.

The section also co-sponsored with the FDA Statistical Association a 2 day workshop on Statistically Sound Decision Making that was held in September. The program committee organized a comprehensive and attractive program featuring 11 sessions. The meeting had record attendance with over 350 registrants. The Drug Information Journal has invited submission of papers from the workshop for a special issue on biomedical statistics. Special thanks go to the co-chairs Greg Campbell and Sandy Heft and their large organizing committee for their outstanding efforts.

A number of years ago the section implemented a number of measures to reduce our budget surplus to more reasonable levels. However this resulted by the end of 1999 in available funds that was somewhat less than our annual operating budget. This required the section to pay closer attention to our expenses and revenues. We instituted a number of modest initiatives that appears to have resulted in the section nearly breaking even in 2000. However, we will need to continue to carefully monitor our budgetary process. Much thanks go to Sally Greenberg, our secretary/treasurer, for keeping on top of this important activity. Sally's work commitments made it difficult for her to carry out her secretarial duties. These duties were delegated to Ram Suresh, whom I would like to thank for his efforts.

The section published several issues of our Biopharmaceutical Report. In my view this report is one of the most important services that we provide our members. My thanks go to Demissie Alemayehu, Ersen Arseven, and Kannan Natarajan for their hard work in maintaining the high standards of this report. Featured articles included: Data Safety Monitoring Boards: An Introduction, and Knowledge Discovery from Data-bases and Data Mining: New Paradigms for Statistics and Data Analysis? Denise Roe, our publication officer, should be thanked for her continuing efforts in coordinating out section proceedings that contained papers of 1999 and the information articles more fully describing section activities which appeared in nearly every issue of *Amstat News*.

Section membership remains over 2000. In addition to providing the traditional services, the membership committee (David Carlin (chair), Bruce Binkowitz, Christine Clark, and Lakshmi Vishnuvajala) is developing a questionnaire to assess member satisfaction and to identify important membership issues that will hopefully be implemented in 2001. The committee also has been working diligently

behind the scenes with the ASA office to resolve some frustrating problems that we've had with our membership and mailing lists. On behalf of the section, I apologize for any inconvenience that these problems have caused our members but please be assured that we are aware of the problems and have been attempting to resolve them.

Sally Greenberg is also moderator the electronic discussion group list that provides an online forum for interesting discussion on a number of interesting topics. She capably handled several maintenance issues that arose this year. Thanks also goes to Kaylan Ghosh who maintained our web site (www.best.com/~asabp/index.htm.) This site is source of much useful information including minutes of section meetings and past issues of the biopharmaceutical report.

The section also had liaisons with PhRMA (Ken Resser), the Deming Applied Statistics Conference (Kaylan Ghosh), and the Midwest Biopharmaceutical Statistics Workshop (Ken Gerald).

Thanks go to our Council of Section Representatives Nancy Smith and Ralph Harkins and Kathy Monti who served on our Executive Committee. Thanks also go to our Fellows Nomination Committee (Larry Gould, Bruce Rodda, and Charles Goldsmith) for their 2000 campaign efforts.

I would like to especially thank Steve Snapinn for his many years of dedicated outstanding service to the Section. Steve was a former program chair, 1999 section chair. This year, as past chair, Steve was responsible for forming the strong slate of candidates for offices that will be elected in 2001. I only hope that I can as equally well as Steve.

As Steve Snapinn promised last year in his outgoing chair message, Bob Davis was to prepare for *Biopharmaceutical Report* an official history of the section that was to be "informative, entertaining, and irreverent". I would be remiss in my duties if I did not report that we were unable to meet this objective. It seems that Bob, who is getting along in years, either had a difficult time remembering to do this or has lost some of his edge thereby finding it difficult to achieve the promised entertaining and irreverent flavor of the historical document.

As this summary indicates, the section once again had a strong and vibrant year. The members of the section's executive and awards committee, session organizers and chairs, presenters, and many other volunteers are to be congratulated for a job well done. The section will certainly continue its excellent service under the direction of Jeff Meeker who is the 2001 section chair. The following individuals were elected officers of the section with terms beginning in 2001: Chair Elect-Robert Small, Program Chair Elect-Leonard Oppenheimer, Council of Section Representative-Avital Cnaan, and Publications Officer-Demissie Alemayehu. Elsewhere in this report, Jeff Meeker will announce appointed committee members and their responsibilities.

I enjoyed serving as section chair and wish everyone the best during 2001.

Looking Ahead to 2001

Jeff B. Meeker

Bristol-Myers Squibb Co.

Again, there is an excellent group of volunteers who will lead the Section for 2001, starting off with the elected positions: Robert Small as Chair Elect; Leonard Oppenheimer as Program Chair Elect; Avital Cnaan as Council of Sections Representative; and Demissie Alemayehu who steps into the Publications Officer position. Continuing are Tom Capizzi as Past Chair and Chair of the Nominating Committee and Keith Soper moves to Program Chair.

Greg Campbell, David Carlin, Lukas Makris, and Kathy Monti remain on the Executive Committee and will be joined by Tom Bradstreet and Anne Cross.

The Section's scientific program is in excellent hands. In addition to Bob Small and Lenny Oppenheimer, Greg Enas has agreed to be the Section's co-chair for the workshop with the FDA and he is gathering his own committee. Kathy Monti has already started putting together the Round Tables for the JSM.

Tom Bradstreet has become chair of the Student Paper Committee and will be helped by Christine Clark, Sanat Sarkar, and Margaret Minkwitz. The Contributed paper award will be handled by Anne Cross. She is working to find others to help gather and process the data.

Demissie Alemayehu is moving into past editor of the Biopharmaceutical Report (along with his duties as Publications Officer). Kannan Natarajan takes over as editor. He will be helped by the new Associate Editor, Neal Thomas.

David Carlin has agreed to stay on for one more year as Chair of the Membership Committee. Bruce Binkowitz, Bill Myers, and Christine Clark continue on the Committee. Newly appointed is Marci Levenstein.

The Fellows Committee has been completely revamped this year and a three-year rotation has been initiated. Bob Davis has agreed to be on the Committee for one year and to be its chair. Bob Starbuck will serve a two-year term and Christie Chuang-Stein is appointed for a three year term. Kalyan Ghosh remains our Webmaster and Sally Greenberg remains Mail List Coordinator.

This is an excellent list of people to lead the Section and its activities during 2001. I look forward to another outstanding year for the Section. I know there were many others who indicated they were interested in volunteering for the Section and there are still places where people can contribute. For this year, you can contact the Chair for the area of interest. Also, Bob Small is making appointments this year for 2002 and beyond.

As a last remark, I want to thank Tom Capizzi for being Chair during 2000. The chair's contribution is important: he's the one that keeps all this going. He did an excellent job and we had a good year. Thank you, Tom.

Section News

Summary of Minutes Of ASA Biopharmaceutical Section

Transition Meeting-November 1, 2000

Tom Capizzi

Merck Research Laboratories

Attendees: Tom Bradstreet, Greg Campbell, Bob Small, Sally Greenberg, Jeff Meeker, Tom Capizzi, Keith Soper, Ram Suresh, Steve Snappin, David Carlin, Anne Cross, Nancy Hiatt (ASA office), Nancy Smith, Mary Fleming (ASA office).

For the 2000 JSM, arrangements, equipment, overall turnout for the sessions/ short courses, were very good. The questionnaires handed out at the JSM sessions were tabulated using the current guidelines and the results were presented. The winners will be announced during the first quarter of 2001.

Registration for the 2000 Workshop exceeded 350. Drug Information Journal has agreed to publish the papers presented at the workshop. Speakers have been notified of the opportunity. The workshop lost \$500 approximately. An increase in the 2001 registration fee was discussed.

The current issue of the Biopharmaceutical report has been mailed to the members recently. The next issue will be in the first quarter of 2001. The option of on-line publication of Biopharmaceutical report was discussed.

A new membership survey for next year will be developed. The existing survey would be shortened and focus on obtaining information regarding the interests of members. Feasibility of web-based survey would be explored.

Reports on the financial status as of 9/30/2000 were presented by Sally Greenberg. A draft 2001 budget was also presented. The 2001 budget was approved with changes.

It was noted that the electronic discussion list will no longer be supported by the vendor. The difficulty in obtaining a current electronic list of members was also noted. The ASA office promised more timely membership lists. The ASA may also be in a better position now than in the past to support mailing lists and web pages. We will ask ASA for help in these efforts. Other options will also be explored for the electronic discussion list.

Keith Soper reported that, out of the nine proposals submitted for invited sessions, five were selected to be featured in the 2001 JSM.

Tom Bradstreet, the sub-committee, noted that student awards will be publicized in *Amstat News* and *Biopharmaceutical Report*. In order to encourage participation, schools will be contacted.

Jeff Meeker announced the following additional appointments: Greg Enas (workshop), Cathy Monti

(roundtable coordinator), Anne Cross (contributed paper). Jeff noted that the membership committee still has an open position.

A total of four packages, 3 new submissions & 1 re-submission, have been prepared by the fellows committee that is chaired by Bob Davis.

The committee agreed to support the efforts of the Princeton-Trenton Chapter in organizing a one-day course on Equivalence.

Tom Capizzi will present a revision of the Manual of Operations at the first 2001 Executive Committee meeting that will be held at the ENAR spring meeting.

The committee members recognized and thanked Steve Snappin for all the services he rendered as an executive committee member.

ENAR 2001 Biopharm Sessions

Samuel M. Heft

Schering-Plough Research

The ENAR 2001 Spring Meeting will be held March 25–28 at the Hilton Charlotte and Towers and the Charlotte Convention Center in Charlotte, North Carolina. The Impact of Technology on Biometrics is the theme for this year's meeting. Carol Gotway Crawford and the program committee have developed an exciting program that reflects the broad range of interests in our membership. Dr. Daryl Pregibon of AT&T Shannon Research Labs will deliver the 2001 Presidential Invited Address. Beverly Mellen of Wake Forest University School of Medicine is the local arrangement chair and planning unique and fun things to do in Charlotte, including a trip to the NASCAR Speedway. We hope to see you in Charlotte.

Two sessions will be sponsored by the Biopharmaceutics Section at the ENAR 2001 meeting:

- (1) "The Value and the Issues of Dynamic Randomization", organized by Corsee Sanders, Genentech, Inc. This session has been designated as one of five invited theme sessions; the theme is "The Impact of Technology on Biometrics".
- (2) "Statistics in Pharmacogenomics, Genomics, Proteomics", organized by Gerald Hajian, Schering-Plough and Stan Young, Glaxo-Wellcome.

In addition, we will be the co-sponsor of three sessions:

- (1) "Modern Experimental Design for Biopharmaceutical Research", organized by Mary Foulkes, FDA
- (2) "Positive Control Studies: US and EC Perspectives", organized by James Schwenke, Covance, Anna Nevius, FDA/CVM, and Robert C. Condon, RJC Associates
- (3) "Role of Statistics in Vaccine Initiatives", organized by M. Elizabeth Halloran, Emory University.

Annual FDA/Industry Workshop: Statistically Sound Decision Making

Gregory Campbell

FDA, Center for Devices & Radiologic Health

Sandy Heft

Schering-Plough Research

The annual FDA/Industry Workshop, which is cosponsored by the ASA Biopharmaceutical Section and the Food and Drug Administration Statistical Association, was held September 14-15, 2000 at the Hyatt Regency in Bethesda, Maryland. Attendance was excellent, with 360 registrants from the FDA, pharmaceutical industry, CRO's, and academia. This workshop offers a chance to exchange views informally from a broad range of people from all the represented areas.

The Program co-chairs were Greg Campbell from the FDA and Sandy Heft from Schering-Plough. The rest of the Program Committee included: Satish Misra, Stella Machado, Bob O'Neill, Chuck Anello, Gene Pennello, Anna Nevius, and Kooros Mahjoub from the FDA, and Walt Offen (Lilly), Kannan Natarajan (Bristol-Myers Squibb), Greg Enas (Lilly), Ram Suresh (Schering-Plough), Michael Chernick (Biosense-Webster), Bob Starbuck (Wyeth-Ayerst), Tony Segreti (Glaxo Wellcome), Devan Mehrotra (Merck), and Kevin Anderson.

The first day included four sessions: "Superiority/Non-inferiority", "Multiple Data Imputation", "Computer Intensive Methods", and "Rational Drug Development". On the second day, the morning used a new format based on the theme of "Alternative Study Design and Analysis": first there was a plenary session with two speakers, Steve Goodman from Johns Hopkins "Bayesian/Likelihood Alternatives to Traditional Measures of Evidence" and Bill Rosenberger from the University of Maryland "Ethics and Alternatives in the Design of Clinical Trials". Then there were three parallel sessions: "Clinical Applications of Alternative Design & Analyses Methods", "Nonclinical Applications of Alternative Design and Analysis", and "Postmarketing Surveillance and Health Outcomes". In the afternoon, there likewise were three parallel sessions: "Multiple Comparisons", "Statistical Consulting", and "Issues with Stratification in Clinical Trials".

All the sessions were extremely well organized and conducted, tribute to the session chairs and speakers, emphasizing applications, and generally including speakers from both the FDA and Industry.

2000 ASA Fellows

Robert L. Davis

AstraZeneca L.P.

Larry Gould

Merck Research Laboratories

The Biopharmaceutical Section is pushing to get members of the section elected Fellows of the ASA, since there are many Section members whose contributions to the profession and to society merit this honor. One way that we can achieve success is by each of you thinking about one or more colleagues who would merit nomination for Fellowship. You can include yourself, by the way. The process by which Fellow nominations are put together is not difficult, and there are hints that people who have put successful nominations together can provide that may be helpful. The Fellows Committee was created by the Section to help you identify worthy candidates and to help with putting a nomination together.

If you have a suggested nominee or need more information, please contact:

Robert L. Davis
725 Chesterbrook Boulevard
Mail Stop A-3E
Wayne, PA 19087-5677
Phone: (610) 695-1070
Email: bob.davis@astrazeneca.com

Guidelines for justification or nomination packages may also be obtained at <http://www.amstat.org/fellows>.

56th Deming Conference

Note: The Conference has been postponed to April 23–27, 2001

The Metropolitan Section of the American Society for Quality in conjunction with the American Statistical Association's Bio-Pharmaceutical Division and the Statistics Division of the American Society for Quality sponsors the 56th Deming Conference. The Millennium Deming conference will be held from April 23rd to 27th, 2001 at the Holiday Inn North Hotel at Newark Airport. The first row of each day are the 3 hour morning sessions, from 8:30 am to 11:30 am, the second row, the 3 hour afternoon sessions from 1:00 pm to 4:00 pm. Lunch is included with the registration.

Revised Conference Outline

Monday, April 23th

A.M.

Dr. Jose Pinheiro,
Bell Labs., Lucent Technologies
Prof. Douglas Bates,
University of Wisconsin
Mixed Effects Models in Sand S-Plus*

Prof. Heping Zhang,
Yale University School of Medicine
Recursive Partitioning in the Health Sciences with Emphasis on Genetic Studies*

Dr. Ronald D. Snee,
Six Sigma Breakthrough Technology
Dr. Roger W. Hoerl,
General Electric
Statistical Thinking and Six Sigma

P.M.

Prof. J. Start Hunter,
Princeton University
The Box-Jenkins Manual Adjustment Chart*

Dr. Keith Soper,
Merck Research Laboratories
Recent Advances in Analysis of Animal Studies of Pharmaceutical Safety

Mr. Greg Gruska,
The Third Generation, Inc
Six Sigma: Silver Bullet or Empty Promises

Tuesday, April 24th**A.M.**

Prof. C. F. Jeff Wu,
The University of Michigan
**Experiments: Planning, Analysis, and
 Parameter Design Optimization***

Dr. Richard Entsuaah,
Wyeth-Ayerst Research
**ETRANK Procedure an Alternative Approach to
 Parametric Methods in Handling Missing Data**

Mr. Barry Graziano,
Bracco Diagnostic
Leadership And Organizational Energy

Mr. Edwin S. Shecter,
TQRI
Management of the Quality Function

P.M.

Prof. John M. Lachin,
George Washington University
**Biostatistical Methods: The Assessment of
 Relative Risks***

Phillip God,
Talus Solutions
Permutation Tests*

Dr. David Laney,
Bell South
If you ain't Doin' Statistics, You ain't Doin' Quality

Wednesday, April 25th**A.M.**

Prof. David W. Hosmer, Jr.,
University of Massachusetts
Applied Survival Analysis*

Dr. Cyrus R. Mehta,
Cytel Software Corporation
**Group-Sequential Inference and Interim
 Monitoring with EaSt-2000**

Prof. Tom Barker,
Rochester Institute of Technology
Introduction to Robust Design

P.M.

Prof. Samprit Chatterjee,
New York University
Regression Analysis by Example*

**Begin Short Course on Resampling Methods:
 A Guide for Practitioners**

Prof. Joyce Nilsson Orsini, *Deming Scholars MBA
 Program at Fordham University/ W.E. Deming Institute*
Hands on Sampling

Short Courses, April 26th & April 27th

Dr. Phillip Good,
Talus Solutions
 Mr. Michael Chernick,
Biosense Webster
 Dr. Cyrus R Mehta,
Cytel Software Corporation
Resampling Methods: Guide for Practitioners

Prof. William J. Latzko,
Fordham University/Latzko Associates
An Overview of Dr. Deming's Principles*

* An asterisk following a title indicates talk based on text sold at the Conference at Discount.

Those wishing to obtain additional information about the program and registration form may do so by contacting: Walter Young, P.O. Box 42528, Philadelphia, PA 19101-2528. Voice: 610/341-5640, Fax: 610/989-455, E-mail: YoungW@war.wyeth.com after August.

Twenty-Fourth Annual Midwest Biopharmaceutical Statistics Workshop

**Monday, May 21-Wednesday, May 23
 Muncie, Indiana**

The workshop will be held on the campus of Ball State University in Muncie, Indiana. It is co-sponsored by Ball State University and the Biopharmaceutical Section of the American Statistical Association. A preliminary program is shown in the February *Amstat News*. For more information contact the Publicity Chair John Schollenberger, Quintiles, Inc., phone (816) 767-6717, Email john.schollenberger@quintiles.com; Stacy David, Program Chair, Eli Lilly and Co., phone (317) 277-5399, Email David_Stacy@lilly.com; or Mir Ali, Local Arrangements Chair, Ball State University, phone (765) 285-8670, Email MALI@wp.bsu.edu.

For more information: www.cs.bsu.edu/homepages/ali/mbsw24.html.

Biopharmaceutical Section Executive Committee, Representatives, and Functions (2000)

Immediate Past Chair

Steven M. Snapinn, Ph.D.
Senior Director, Scientific Staff
Merck Research Laboratories

Chair

Thomas Capizzi, Ph.D.
Senior Director
Merck Research Laboratories

Chair Elect

Jeff B. Meeker
Bristol-Myers Squibb Co.

Secretary Treasurer

Sally A. Greenberg, Ph.D. (1999-2001)
Director, Biostatistics
COR Therapeutics, Inc.

Program Chair

Robert D. Small, Ph.D.
Pfizer, Inc.

Program Chair Elect

Keith A. Soper
Merck & Co. Inc

Publications Officer

Denise J. Roe, Dr. P.H. (1997-2000)
Research Associate Professor
University of Arizona

Publications Officer Elect

Demissie Alemayehu, Ph.D. (2001-2003)
Biometrics Director
Pfizer, Inc.

Council of Sections Representative

Nancy Smith (1999-2001)
Office of Training and Communications
FDA

Ralph D. Harkins, Ph.D. (1998-2000)
Vice President,
Biometrics and Clinical Data Management
Target Research Associates

Executive Committee Members

Katherine L. Monti, Ph.D (2000-2002)
Rho, Inc.

Lukas Makris, Ph.D. (1999-2001)
BioCor, L.L.C.

Demissie Alemayehu, Ph.D. (1997-2000)
Biometrics Director
Pfizer, Inc.

Avital Cnaan, Ph.D. (1998-2000)
Director, Div. of Biostatistics and Epidemiology
Children's Hospital of Philadelphia

David A. Carlin (1998-2000)
Vice President
Biostatistics & Data Management
MedImmune Inc

Gregory Campbell
FDA
Center for Devices & Radiologic Health

Section Co-Chair 2000 FDA/Industry Meeting

Samuel M. Heft, Ph.D. (1997-2000)
Senior Director, Statistics
Schering-Plough Research Institute

Biopharmaceutical Report Editors

Demissie Alemayehu, Ph.D. (1997-2001)
Biometrics Director
Pfizer Inc.

Kannan Natarajan, Ph.D (2000-2002)
Bristol Myers Squibb

Ersen Arseven, Ph.D. (1998-2000)
President
Arseven Consulting, Inc.

Membership Committee Chair

David A. Carlin (1998-2000)
Vice President, Biostatistics & Data Management
MedImmune Inc.

Membership Committee Members

R. Lakshmi Vishnuvajjala (2000-2002)
FDA
Center for Devices & Radiologic Health

B. Christine Clark (2000-2002)
Sr. Director Operations,
Biometrics IBAH, Inc.

Bruce Binkowitz (2000-2002)
Merck & Co, Inc.

William R. Myers (2000-2001)
Proctor & Gamble Pharmaceuticals
Health Care Research Center

Fellows Nomination Committee

A. Lawrence Gould, Ph.D.
Merck Research Laboratories

Charlie H. Goldsmith
Centre for Evaluation Medicine
St Joseph's Hospital
McMaster University

Bruce E. Rodda, Ph.D.
PPD Pharmaco

2000 JSM Roundtable Coordinator

Lukas Makris, Ph.D. (1999-2001)
BioCor, L.L.C.

**Liaison to Midwest Biopharmaceutical
Statistics Workshop**

Ken Gerald
Applied Logic Associates

**Webmaster/Liaison to Applied Statistic
Conference**

Kalyan Ghosh, Ph.D.
Merck Research Laboratories

**Liaison to PhRMA Biostatistics Steering
Committee**

Kenneth J. Resser
Director, Biostatistics
Amgen Inc.

Student Paper Competition Chair

Avital Cnaan, Ph.D. (1998-2000)
Director, Div. of Biostatistics and Epidemiology
Children's Hospital of Philadelphia

**2000 JSM Contributed Paper Award
Committee**

Thomas E. Bradstreet, Ph.D.
Merck Research Labs

Sanat K. Sarkar, Ph.D.
Temple University

Douglas Faries
Research Scientist
Lilly Research Laboratories

Viswanath Devanarayan
Senior Scientist
Lilly Research Laboratories

Let's Hear from You!

If you have any comments or contributions, contact Editor Demissie Alemayehu, Biometrics Director, 235 East 42nd Street, Bldg 205/4, Pfizer Inc, New York, NY 10017; e-mail: alemad@pfizer.com; Associate Editor Kannan Natarajan, Bristol Myers Squibb, P.O.Box 5400, Princeton, NJ 08543; Phone: 609-818-4299; Fax: 609-818-5740; e-mail: Kannan.Natarajan@bms.com ; or Past Editor Ersen Arseven, Arseven Consulting, Inc., 55 Old Nyack Turnpike., Suite 606, Nanuet, NY 10954; Phone: 845-627-1321; e-mail: earseven@spyral.net.

The *Biopharmaceutical Report* is a publication of the Biopharmaceutical Section of the American Statistical Association.

(c) 2000 The American Statistical Association
Printed in the United States of America

NON-PROFIT ORG
U.S. POSTAGE
PAID
ALEXANDRIA, VA
PERMIT NO. 361

Biopharmaceutical Report
c/o American Statistical Association
1429 Duke Street
Alexandria, VA 22314-3415
USA

