Model-Based Drug Development Survey Finds Pharmacometrics Impacting Decision Making in the Pharmaceutical Industry

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During the past decade, the pharmaceutical industry has seen the increasing application of pharmacometrics approaches in drug development. However, the full potential of incorporating model-based approaches in drug development and its impact on decision making has not been fully realized to date. In 2009, a survey on model-based drug development (MBDD) was conducted (1) to further understand the current state of MBDD in the pharmaceutical industry and (2) to identify opportunities to realize the full potential of MBDD. Ten large and mid-sized pharmaceutical companies provided responses to this survey. The results indicate that MBDD is achieving broad application in early and late development and is positively affecting both internal and regulatory decisions. Senior leadership (vice president and higher) within the companies indicated widely accepted utility for dose selection and gaining acceptance for study design and regulatory interactions but limited acceptance in discovery and commercial/pipeline decisions. Mounting appreciation for the impact of MBDD on internal and regulatory decision-making bodes well for the future of the pharmacometric discipline and the growth of opportunities to realize the full potential of MBDD.

Keywords: *Pharmacometrics; modeling; simulation; model-based drug development; pharmaceutical industry*

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The past decade has seen the increasing application of pharmacometric (interchangable with modeling and simulation) approaches in drug development and a shift from empiric to model-based drug development (MBDD) in much of the pharmaceutical industry. This shift also corresponds to the use and interest in model-based approaches by regulators.[1-4] However, the full potential of incorporating model-based approaches in drug development and its impact on decision making is not fully understood, nor has the current state of MBDD within the industry relative to this full potential been fully examined. Concept articles from academic groups have provided the theoretical basis for the role of model-based approaches in drug development,[5-8] and more recently, articles have described the impact and future potential of MBDD based on the experience of individual companies.[9-12] This white paper presents a cross-industry perspective of the recent and future utility of MBDD as obtained through an industry survey conducted in August and September 2009. Through this survey, the perspective of the industry pharmacometrics groups and their key internal customers of MBDD were explored through a series of semiquantitative and qualitative questions. It is hoped that the collected information presented here will be useful for advocacy purposes both within industry and also more broadly across the emerging pharmacometrics discipline.

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SURVEY

This survey was developed in 2009 by the Model-Based Drug Development (MBDD) Initiative group,

which was originally a subgroup of the Pharmaceutical Research and Manufacturers of America (PhRMA) organization's Clinical Pharmacology Technical Group (CPTG). The survey questions were based on feedback and individual experiences with MBDD within the organizations of the MBDD group members, as represented by this white paper's authorship. The survey was reviewed by the PhRMA organization, including a legal review to ensure that it was in compliance with all PhRMA policies and procedures. The survey was conducted using SurveyMonkey's Web-based survey technology and was distributed to the members of the CPTG as points of contact within their respective companies. Only 1 survey response per company was collected, and respondents were asked to reflect the aggregate of all modeling and simulation groups active in research in their companies in their responses. Responses to the survey were received by a PhRMA staff member, who ensured that all information collected was aggregated and blinded upon receipt.

The survey was composed of 36 questions divided into 4 sections: section 1 contained 2 questions on the overall company. Section 2 was the largest section and contained more detailed questions on pharmacometrics. Section 3 contained 7 questions intended to characterize the perception of MBDD and its value in drug development by the key internal customers of pharmacometrics within the respondent company. It was requested that the respondent ask up to 3 senior leaders (within 2 levels of the head of research) who head groups that use the pharmacometrics results within their company to complete these questions. A final section (section 4) provided an optional write-in section for provision of any comments on any questions or to expand on themes not specifically addressed in the specific multiple-choice questions in sections 1 to 3.

Following a reorganization within PhRMA that led to the discontinuation of standing working groups such as CPTG that occurred after administration of the survey but prior to the final analysis for this white paper, the survey data were sent in a blinded fashion to the authors to preserve the anonymity of the individual responders and to allow completion of the analysis. The survey was originally sent to the 14 PhRMA member companies with representation on the CPTG. Of the 14 companies sent the survey, 11 companies completed the original survey for a 79% response rate, and 10 companies provided permission for their responses to be used for this article.

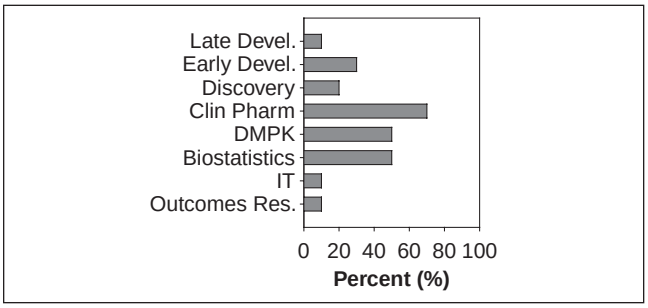

Figure 1. Location of pharmacometrics group(s) in the overall research organization.

RESULTS AND DISCUSSION

Of the 10 responder companies represented in the survey results, 7 were large companies with >15 000 employees and 3 were mid-sized companies with between 1000 and 15 000 employees. All were active in branded small molecules, 2 in generic small molecules, 7 in branded biologics, 4 in follow-on biologics, 5 in over-the-counter and consumer products, and 4 in vaccines. In this section, the results from the survey questions will be provided and discussed in 7 sections: (1) Organizational Structure for Pharmacometrics, (2) Staff and Skill Sets for Pharmacometrics, (*3*) Types of Pharmacometrics Activities, (4) Internal and External Partners, (*5*) Strategy Development and Integration With Overall Development, (6) Impact of MBDD and Metrics, and (7) Senior Leadership Perspective.

Organizational Structure for Pharmacometrics

Three questions addressed organizational structure for pharmacometrics. Most (9) respondents indicated that there were multiple pharmacometrics groups within their companies, with 5 indicating the multiple groups had separate management, 3 indicating the multiple groups were within various functions, and 1 indicating the multiple groups were aligned by therapeutic area. One respondent indicated that pharmacometrics was supported by a single group within their company. Figure 1 displays the location of the pharmacometrics group(s) in the overall research organizations. A wide variety of locations were noted, with clinical pharmacology, drug metabolism and pharmacokinetics (DMPK), and biostatistics being the most common locations for pharmacometrics. The reporting levels of the pharmacometrics organizations within the companies

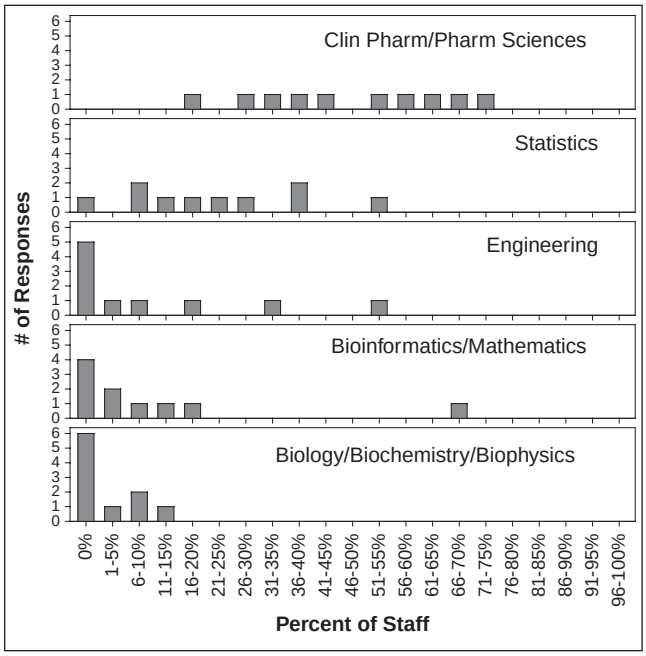

Figure 2. Pharmacometrics staff members' education and training background by various scientific disciplines.

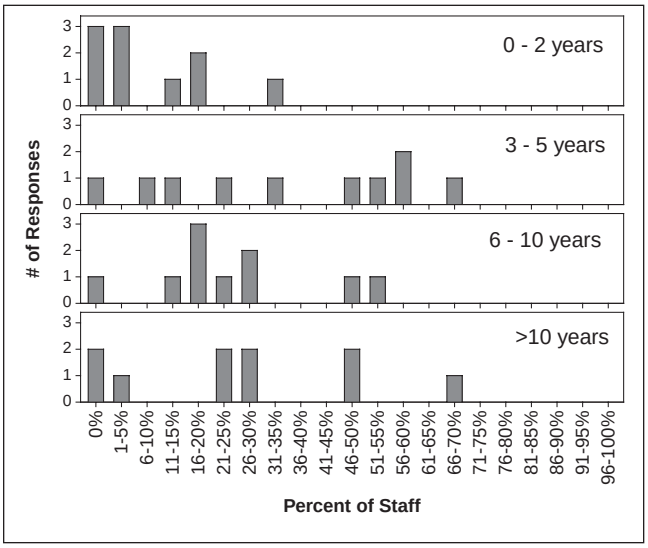

Figure 3. Pharmacometrics staff members' years of postdegree experience.

were consistent with the locations (2 to head of early development, 5 to head of clinical pharmacology, 3 to head of DMPK, 3 to head of biostatistics, 1 to head of quantitative sciences) and in most cases reflected pharmacometrics as reporting through another traditional drug development field rather than directly into a more cross-disciplinary level of research management. This may reflect a still-emerging nature of the pharmacometrics discipline and also parallels current academic structures for training scientists within this field (largely within related disciplines), as examined further in the next section. At the same time, it is encouraging to observe that pharmacometrics functions are reporting to the head of early development at 2 companies and that more senior-level positions for pharmacometrics functions have been created recently (eg, executive director– or vice president–level positions). Both enhanced leadership levels and more strategic positioning of pharmacometrics functions indicate that pharmacometrics is increasingly considered to be a discipline that affects decision making rather than a solely technical discipline in research and development. This direction in industry parallels the enhanced role of pharmacometrics in regulatory groups such as the US Food and Drug Administration (FDA).

Staff and Skill Sets for Pharmacometrics

Four questions addressed staff and skill sets available within industry pharmacometrics groups. Among the large-company respondents, 3 employed 10 to 20 pharmacometrics staff members, 2 had 20 to 40 staff members, and 2 had >40 staff members. For the mid-size companies, one employed 1 to 3 staff members and two had 10 to 20 pharmacometrics staff members. Further questions examined the skill sets and educational background of the staff composing the pharmacometrics groups in these companies. Figure 2 illustrates the educational background and Figure 3 the years of experience of the pharmacometrics staff members. The highest degree of the staff members was also examined. In all companies, most of the staff were PhD-level (4 with 51%-60%, 1 with 61%-70%, 1 with 71%-80%, 4 with >90%) with few MD-level staff members (7 with 0%, 3 with 1%-10%). The proportion of MS-level staff ranged fairly widely, from 0% to 40% (4 with 10% or less, 1 with 11%-20%, 2 with 21%-30%, 3 with 31%-40%). All companies reported few BS-level staff (4 with 0%, 4 with 1%-10%, 2 with 11%-20%). These results would appear to reflect that for most pharmacometrics roles, some advanced education and training is viewed as necessary within industry.

Overall, the responses on background of the pharmacometrics staff reflect considerable diversity of educational background in staff supporting

pharmacometrics within industry, with half the respondents reporting most staff from the clinical pharmacology/pharmaceutical science field. However, for 5 respondents, staff from this field was in the minority of staff supporting pharmacometrics. For 1 respondent company each, most of their pharmacometrics staff members had a background in statistics, engineering, or bioinformatics/mathematics. In most companies, statistics backgrounds were well represented in the pharmacometrics groups, and for several companies, engineering backgrounds were substantively represented. These results can be viewed as reflecting strength derived from a multidisciplinary perspective as well as recognition that a variety of academic fields provide an appropriate background for industry pharmacometrics support.

The results for years of experience reflect a wealth of longer-term experience available within most pharmacometrics groups, with a tendency for few staff with <2 years of experience (Figure 3). In discussion, the diversity of lengths of tenure could indicate the initial migration of industry-experienced scientists into this field in the early years, with some maturation over time during the years of slow growth, and now, as this becomes an emerging field with renewed interest and emphasis, the range of newer staff will begin to present in most pharmacometrics groups. This is consistent with the relatively small number of staff with <2 years of experience in what is often seen as a growth area within the pharmaceutical industry. It might also reflect that most scientists do not directly hire into pharmacometrics groups but rather begin their industry careers in related disciplines to gain drug development experience before joining the pharmacometrics groups.

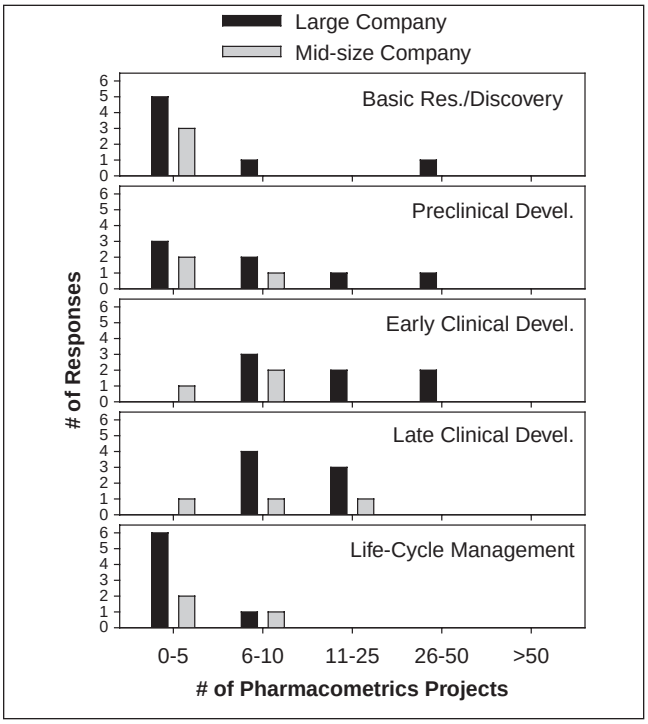

Figure 4. Number of pharmacometrics projects completed in 2008 by development phase.

Types of Pharmacometrics Activities

Six questions addressed the types and quantity of pharmacometrics activities conducted within the companies. Figure 4 provides the number of pharmacometrics projects completed in 2008 by development phase, where project was defined as a completed model and associated simulation work. The pattern in both the medium-sized and large companies is similar. The greatest number of complete projects is found in the early and late clinical development phases, with some companies also reporting a sizable number of projects in the preclinical development phase. In general, few projects were completed in the discovery and life-cycle management phases, although 1 respondent noted considerable discovery activity. These results may reflect an expansion of pharmacometrics from a more typical late development and registration support focus prevalent 10 years ago into more extensive use of these approaches in preclinical and early clinical development, likely driven by recognition of the value that pharmacometrics can provide to internal decision making in those earlier phases. However, the limited application in discovery and life-cycle management may reflect reduced applicability but could also potentially reflect a need to further define the role and potential impact of pharmacometrics in those phases. Respondents were also asked to provide the current direction for the level of pharmacometrics activity by development phase within their companies. Anticipated increases in level of activity were broadly noted for earlier phases, with 7 indicating for discovery, basic research, and lead optimization; 10 for preclinical development; 8 for early clinical development; 7 for late clinical development; and 4 for life-cycle management. No company anticipated a decrease in pharmacometrics activity for any phase. These results further support an increased recognition of the value that pharmacometrics can provide to companies in the early development space.

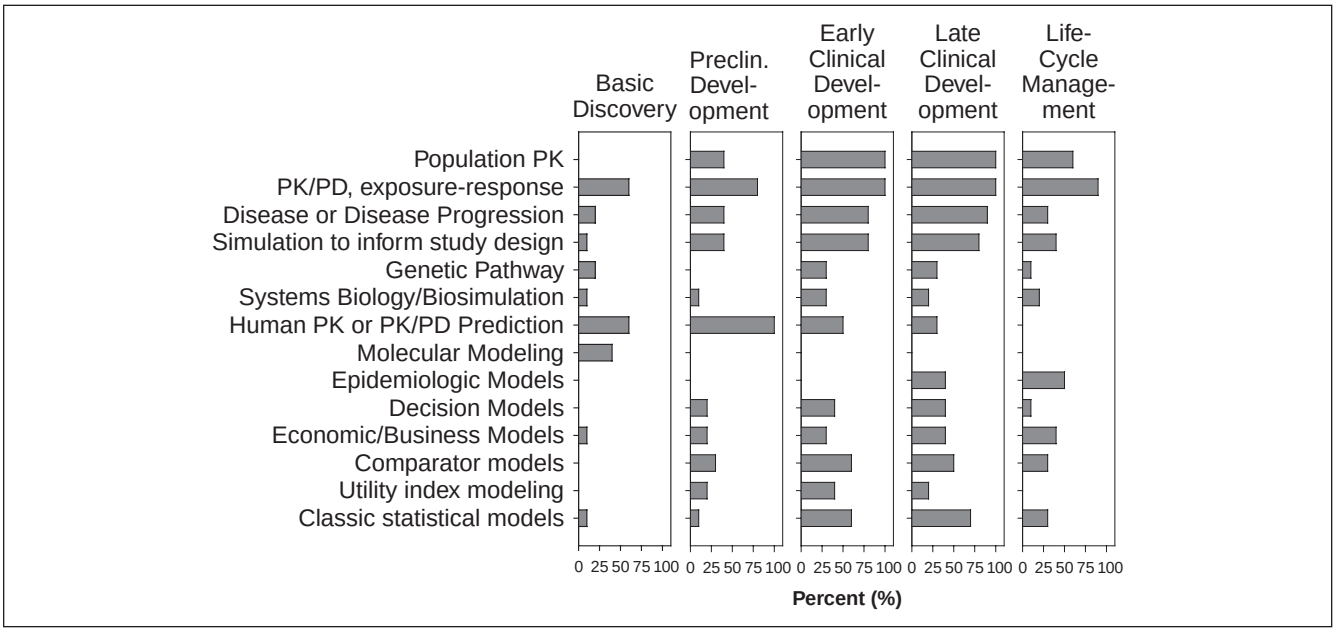

Figure 5. Types of modeling activities conducted and development stage in which employed.

The percentage of current development programs supported with pharmacometrics was estimated at >90% for 1 company, 76% to 90% for 2 companies, 51% to 75% for 4 companies, and 26% to 50% for 3 companies. The distribution in coverage responses was similar in large and mid-sized companies. It is notable that most companies in this survey provided support for most development programs, and this level of coverage likely reflects a growth in support from a more ad hoc application of pharmacometrics that was more common ~10 years ago, as noted from the authors' personal experiences.

Respondents were asked to identify which types of pharmacometrics activities are conducted at their company and in which development phases each specific type of modeling is used. The results are displayed in Figure 5 and indicate broad application of traditional pharmacometrics approaches such as population pharmacokinetics (PK), PK/pharmacodynamics (PD), disease modeling, and trial simulation across the range of development phases with some application in discovery and life-cycle management, particularly for PK/PD. Considerable activity in human PK and PK/PD prediction was identified in discovery and early development. In other areas, including genetic pathway, systems biology, molecular modeling, epidemiology, and classical statistical, much less application was noted, but it is unclear whether this reflects limited use of these approaches in the companies or merely that the modeling groups conducting such work were not well represented by the respondents to the survey. Thus, this may suggest a need to build better bridges and opportunities for cross-communication with such groups to better integrate the pharmacometrics community within the decision-making continuum in pharmaceutical companies. Finally, an encouraging level of application of some of the emerging decision analysis approaches (decision models, economic models, comparator models, and utility index) was noted within the early and late clinical development phases, indicating that multiple companies are at least exploring these approaches. In addition to noting which pharmacometrics activities were conducted, respondents were asked to indicate the current direction for the level of activity of the various modeling types with their companies (Table I). For many of these pharmacometrics activity types, increases in level of usage were anticipated, with PK/PD, trial simulation, and human PK and PK/PD prediction having the largest number of companies anticipating increases. Only 1 company anticipated a decrease in level of usage in any pharmacometrics type, and this was in the area of comparator modeling.

In a question designed to assess whether some therapeutic areas were more readily supported by pharmacometrics than others, respondents were asked to identify therapeutic areas in which their

Table I Current Direction for Level of Pharmacometrics Activity by Modeling Type

Pharmacometrics Activity Type	No. of Companies Anticipating Change From Current State in Level of Activity	
	Increase	Decrease
Population PK	5	0
PK/PD or exposure response	8	0
Disease and disease progression	6	0
Simulations to inform study design	7	0
Genetic pathway	3	0
Systems biology and biosimulation	3	0
Human PK and PK/PD prediction	7	0
Epidemiologic modeling	2	0
Decision models	5	0
Economic or other business models	3	0
Comparator models	5	1
Utility index	4	0
Classical statistical predictive or stochastic models	1	0

company was active and then to indicate whether that area was supported by some pharmacometrics in the company. Table II provides the percentage coverage by pharmacometrics of the therapeutic areas. Many areas had full or high levels of coverage, while some had more moderate coverage (anesthesia, reproductive, rheumatology, and urology) and a few had low coverage (dermatology, gastroenterology, and vaccines). The areas with a lower degree of coverage may reflect more challenge in application of pharmacometrics in these areas, lower perceived potential for impact of pharmacometrics in these areas, fewer regulatory expectations for pharmacometrics in these areas, more limited examples and published disease or therapeutic models in these areas, or some combination of such factors.

Internal and External Partners

Three questions captured information on internal and external partners of pharmacometrics. All companies indicated that biostatistics, clinical pharmacology, DMPK, preclinical PK, discovery/experimental/translational medicine, and clinical development (phase 2/3) were collaborating with pharmacometrics and/or were pharmacometrics group locations. Some respondents also identified collaboration partnerships with early development project team leaders (90%), late development project team leaders (90%), health outcomes/economics (40%), decision/portfolio analysis (30%), safety/epidemiology (40%), and marketing/business (40%). These results reflect that a broad network of collaborations and partnerships generally exists between pharmacometrics and other functional areas within the pharmaceutical companies.

Questions relating to external partners focused on use of pharmacometrics outsourcing. All companies indicated some usage of pharmacometrics outsourcing with 2 companies. Half of the respondent companies indicated pharmacometrics outsourcing utilization of <25%. Of the remainder of the respondent companies, the utilization of outsourcing of pharmacometrics projects was >75% for 2 companies and between 25% and 50% for 3 companies. The most common types of pharmacometrics project work that were outsourced were population PK (100% of respondents indicating some outsourcing of this type) and PK/PD or exposure response (70%). The next most prevalent types of outsourcing were trial simulation (40%), disease and disease progression (30%), comparator models (30%), and economic or other business models (20%). Least common types of outsourcing were systems biology and biosimulation, human PK and PK/PD prediction, epidemiologic modeling, decision models, utility index, classical statistical predictive, or stochastic models (all with 10%). These results reflect a continued important role of pharmacometrics outsourcing in supporting overall pharmacometrics capacity and application in many companies.

MBDD Strategy Development and Integration With Overall Development

Four questions evaluated how pharmacometrics projects are initiated and coordinated within the companies and what efforts are made to develop MBDD strategies for the development program. In initiating pharmacometrics work, a considerable role of collaborative partner groups and leadership was noted by most companies (Table III), with requests by the clinical pharmacology representative on the development team being the most common

Table II Percentage of Therapeutic Areas in Which the Company Is Active That Are Supported by Pharmacometrics Activity

Full Coverage	High Coverage	Moderate Coverage	Low Coverage
100% Allergy	89% Infectious disease	67% Anesthesia	43% Dermatology
100% Blood products	89% Neurology	75% Rheumatology	38% Gastroenterology
100% Psychiatry	86% Pulmonary	67% Urology	20% Vaccines
100% Analgesia	89% Metabolism/endocrinology	67% Reproductive	
100% Cardiovascular	90% Oncology		
100% Nephrology/renal			

route to identification (90% of companies). The pharmacometrics group(s) also plays a role in identification of M&S project work, with 7 of 10 companies reporting that the M&S group leads and/or participates in the identification process. A variety of methods of coordination of modeling work with development project teams was noted (Table III), with a tendency for the pharmacometrics scientist or team representative to be more likely to be a core member of early development project teams but an ad hoc member of late development project teams, perhaps reflecting more of a central focus on pharmacometrics in early development than late, or simply that by late development, project teams have expanded in size such that more aspects are managed through ad hoc memberships and/or subteams. In the responses, a substantive role of pharmacometrics as either core members or leaders of analysis subteams to the project teams was noted. Lastly, a minority of respondents indicated that pharmacometrics did not have a role on early or late development project teams within their companies. Some of these respondents also indicated that sometimes pharmacometrics did have a project team role, suggesting that the role of pharmacometrics with respect to project teams varied on a case-by-case basis within their companies. Two respondents indicated that interactions occurred only through the analysis subteam.

All respondents indicated that they used prospective MBDD strategy plans for development programs within their company, with 2 indicating this always occurs, 2 indicating this regularly occurs, and 6 indicating this sometimes occurs, but not consistently. Respondents were further asked how the MBDD strategy plans were integrated into the overall development plan. Two companies indicated that MBDD strategy is a required section in the overall development plan. Three indicated that MBDD strategy plans are a separate document that is shared widely, and 5 indicated that MBDD strategy plans are primarily used within the pharmacometrics group. Overall, these results reflect that a fair amount of prospective strategic planning for MBDD is ongoing in the pharmaceutical industry but that there may be future opportunities to improve on the consistency of prospective planning and in coordination and alignment

Table III Initiation and Coordination of Pharmacometrics Projects Within a Development Program

How does the pharmacometrics group at your company initiate projects and/or become involved with development project teams?
Requests by:
90% Clinical pharmacology representative
80% Department head or senior leadership
60% Pharmacometrics group leadership
50% Biostatistician
50% Project medical lead
50% Project team leader
40% Franchise/therapeutic area head
30% Project manager
Pharmacometrics group role in pharmacometrics project identification:
60% Pharmacometrics leads process
50% Pharmacometrics participates in process
How does the modeling team interact with the development project team?
Pharmacometrics scientist or pharmacometrics team representative is a:
60% Core member of early project teams
60% Ad hoc member of late project teams
60% Leader of an analysis subteam
50% Core member of an analysis subteam
40% Core member of late project teams
40% Ad hoc member of early project teams
40% Not a member of late project teams
30% Not a member of early project teams

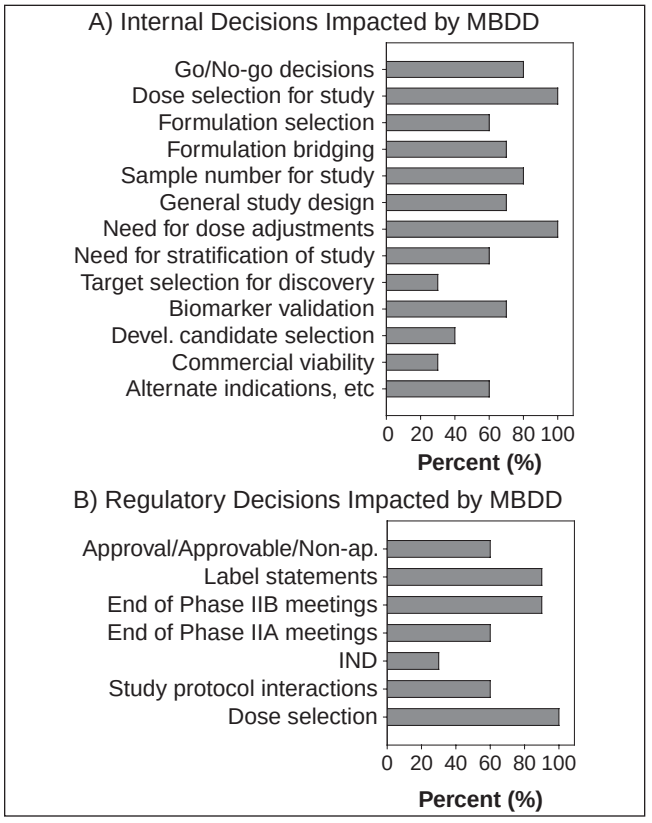

Figure 6. Pharmacometrics group self-assessment of MBDD impact on (A) internal decisions and (B) regulatory interactions.

of MBDD strategy with overall development needs of the project teams.

Impact of MBDD and Metrics

Respondents from the pharmacometrics groups were asked to self-rate where they perceived that MBDD has had an impact both from an internal company perspective and from a regulatory decision perspective (Figure 6). Internally, broad impact was seen on internal decision making in the development phases, with decisions around dose selection and dose modifications being recognized as impacts by all companies and a high proportion of companies also recognizing impacts on study design, go/no-go decisions, and formulation aspects. Impacts were less consistently noted in internal decisions in the discovery support and commercial decision areas. The pharmacometrics groups also perceived that their work had affected regulatory decisions in a number of areas, with regulatory impacts in the areas of dose selection, label statements, and end-of-phase 2 meetings having the broadest recognized impacts (90%-100% of companies). These internally perceived regulatory impacts are consistent with reviews conducted by the FDA Pharmacometrics group to assess the impact that pharmacometrics has had on regulatory decisions, including providing pivotal and supportive information for approval and labeling decisions.[3,4]

Respondents were also asked about what type of metrics their pharmacometrics group tracked and reported to senior management in 2008. The most common metrics were measures of work output (80% of companies) and regulatory impact (50%). A broad range of other metrics was also reported by some of the companies, including measures of internal decisions impact (40%), implementation (40%), financial impact (30%), customer satisfaction (30%), and predictability of projections (30%). Among the 3 companies quantifying financial impact, the estimates for cost avoidance in 2008 were MM$1-5, MM$11-25, and MM$26-100.

Senior Leadership Perspective

The final section of the survey was not completed by the pharmacometrics groups within the companies; rather, it was requested that the respondents identify up to 3 senior leaders within their companies who represented key internal customers to answer 7 questions aimed at gauging their perceptions of MBDD. In total, 17 senior leaders completed this section of the survey, representing 1 chief medical officer, 5 senior vice presidents, and 11 vice presidents. These senior leaders represented a broad range of areas of oversight, with the greatest concentration in the early (12) and late (10) clinical development phases. Additional areas of oversight represented included discovery and basic research (2), preclinical development (4), and postfiling and life-cycle management (6).

The senior leaders were asked to comment on how well MBDD was accepted in their companies for internal decisions in a number of areas. Overall, the results displayed in Figure 7 indicate some acceptance of MBDD for informing most internal decisions, with some interesting patterns in the responses. For dose selection decisions from first-in-humans studies through phase 3 and dose adjustments in subpopulations, all respondents indicated that MBDD was either well accepted or somewhat accepted, and in most cases, the majority felt MBDD was well accepted for these decisions. This result indicates that the case for MBDD informing dose

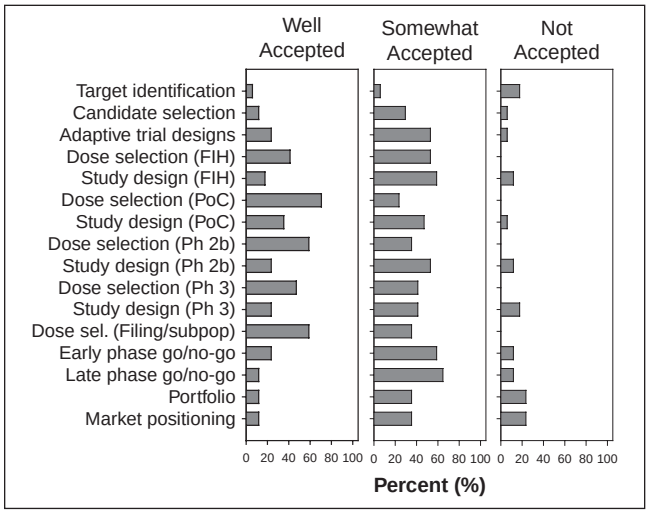

Figure 7. Senior leadership input: acceptability of MBDD for aiding major decisions.

Table IV Senior Leadership Impressions of Utility of MBDD

% Agreement	Statement
71	Essential to maximize success rate of compounds
59	Essential to maximize success rate of filings
53	Essential to maximize benefit/risk for patients
53	Somewhat helpful for internal decision making
41	Somewhat helpful for regulatory decision making
18	Not essential for internal decision making
18	Not essential for regulatory decision making

selection decisions has been broadly accepted within the industry. Further evidence of MBDD gaining acceptance for decisions is also seen in the areas of study design and go/no-go decisions in the development space, as most senior leaders saw these areas as somewhat acceptable to be informed by MBDD, with a few viewing these areas as well accepted and very few seeing these areas as not acceptable for MBDD. In contrast, the results for internal decisions in the discovery (target identification and candidate selection) and commercial (portfolio and marketing positioning) areas suggest that MBDD has further to go in making a case for the utility of MBDD in aiding these decisions. These areas had the lowest responses of well accepted and most of not accepted. Following the question on acceptability for internal decision, if they had indicated not well accepted, the senior leaders were asked to comment on what aspect would need to improve to increase their comfort level with using MBDD to aid decisions. The most common areas for improvements cited by senior leaders were improve timing (59% of senior leaders) and improve communication (59%). In addition, enhanced relevance (41%), more focus on strategic not technical (35%), and better alignment with the project team (35%) were cited areas for improvement. Of note, no senior leader indicated in the survey check box response that better alignment of pharmacometrics with management was needed.

The senior leaders were asked which of a series of statements about the utility of MBDD were consistent with their impressions (Table IV). Encouragingly, most senior leaders saw MBDD as playing an essential role in maximizing the success rate of compounds and regulatory filings and maximizing benefit/risk for patients. However, some senior leaders were still unconvinced of the value of MBDD, as a minority indicated that MBDD was not essential for either internal or regulatory decisions.

The senior leaders were asked to comment on their priorities for MBDD in their companies and their perceptions of where MBDD had had positive impacts within their companies (Figure 8). The top priorities identified were phase 2 decisions, regulatory interactions, and trial simulations, which appear fairly well aligned with the areas of focus and growth of the pharmacometrics groups, as noted in earlier portions of the survey. In the question on positive impacts, dose selection support was seen as the most impactful, consistent with the responses from the senior leaders on acceptability of MBDD for internal decisions. Of note, the influence of MBDD on the scientific and strategic thought process of development project teams was also seen as a positive impact by most senior leaders. It was of interest to see this positive impact noted by senior management, as this day-to-day impact is commonly seen by modelers within their teams, but the extent to which this impact was recognized was less clear. Of more concern was the limited perception by senior management of positive impact in areas such as cost avoidance and labeling, as these impacts are readily translatable to impacts on the bottom line of value derived. Greater perceived impact in these areas

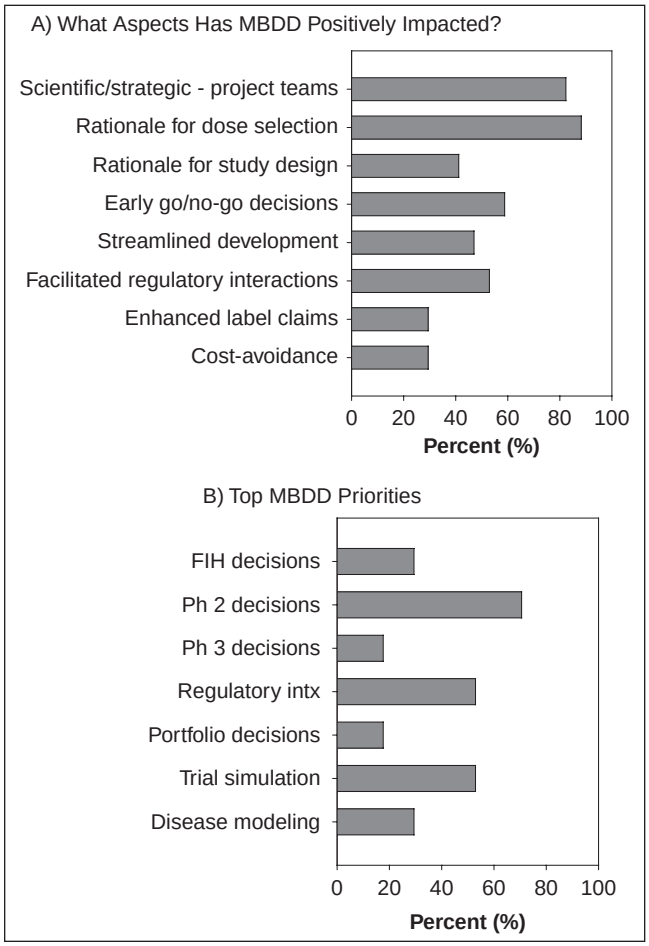

Figure 8. Senior leadership input: positive impacts of MBDD and prioritization of current MBDD needs.

would enhance the ability of pharmacometrics groups to argue for resources in the current resource-constrained environment in the pharmaceutical industry.

Interpretation and Implications

The results from this 2009 survey indicate that pharmacometrics is changing from a solely technical discipline to a discipline that increasingly facilitates and enhances decision making in drug development, consistent with the interpretation from several other articles in this special issue.[13-15] The survey results suggest there has been a broadening and maturation of MBDD within the pharmaceutical industry from a state of more ad hoc and narrow application (eg, population PK) 10 years ago. The results also suggest that further potential gains for drug development are possible from MBDD within the industry. In particular, greater usage and understanding of potential impacts in discovery and very early development and in life-cycle management of mature products would be important. In addition, broadening of the types of MBDD activities pursued and greater alignment and collaboration of pharmacometrics with the wider MBDD community representing a broad diversity of pharmacometrics approaches and applications are other opportunities. Most companies currently have multiple modeling groups within their organization, but given that pharmacometrics activities are generally being conducted through extensive collaboration and partnerships, this may address potential alignment issues. The modeling groups in industry are composed of staff with diverse educational backgrounds and largely advanced degrees (PhD with some MS), with a depth of experienced staff available in most groups. MBDD is currently positively affecting both internal and regulatory decisions, with a particular strength in both level of support and impacts achieved in early and late clinical development. The most commonly cited areas by senior management that need improvement include (1) planning and timeliness of model-based analyses, (2) improved communication about impact of model-based results, (3) enhanced relevance of the models with more focus on strategic and not technical aspects of the models, and (4) improved alignment with project teams and other key stakeholders. Senior leadership within the companies indicated wide acceptance of MBDD to inform dose selection, gaining acceptance for study design and regulatory interactions, but less accepted in discovery and commercial/pipeline decisions.

In conclusion, the survey found that pharmacometrics is affecting decision making in the pharmaceutical industry. Mounting appreciation for the impact of MBDD on internal and regulatory decision making bodes well for the future of the pharmacometrics discipline and the growth of opportunities to realize the full potential of MBDD.

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