LEERINK SWANN

The Healthcare Investment Bank™

Medical Publishing Insights and Practices Initiative

ISMPP Annual Meeting Presentation

April 22nd, 2009

About this Presentation

- This presentation, prepared for the 2009 ISMPP Annual Meeting, summarizes the activities to date of the Medical Publishing Insights and Practices (MPIP) initiative

- The work of the MPIP initiative has been supported by Leerink Swann, an independent consulting firm, from August, 2008, to April, 2009, and the contents of this presentation are valid as of April 22nd, 2009

- The research phase of this work (August – December, 2008) has been conducted under the stewardship of the MPIP Steering Committee, comprised of representatives from Amgen, AstraZeneca, Bristol-Myers Squibb, GlaxoSmithKline, Pfizer and ISMPP

- For more information about this presentation, please contact members of the Leerink Swann team:
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MPIP Goals, Structure and 2008 Activities

MPIP Plans for 2009

The Medical Publishing Insights and Practices initiative is a multi-company project to explore how pharma could develop more effective relationships with journals.

Objectives

- **Understand issues and challenges** facing medical journals in publishing pharma-sponsored manuscripts
- **Identify potential solutions** to increase transparency and trust by promoting more effective partnerships between sponsors and journals
- **Build pharma collaborations** to catalyze future activities to improve pharma-journal relations

MPIP Goals, Structure and 2008 Activities

MPIP Objectives – II

In the long term, this initiative seeks to lay the groundwork for future dialogue and action involving both industries.

Research Phase (2008)	Execution Phase (2009 →)
• Identify key issues from journals' perspective	• Bring together journals and pharma to identify issues of common concern
• Gather journals' ideas for potential solutions to outstanding problems	• Jointly develop and execute solutions to key issues
• Promote open communication between journals and the pharma industry	• Establish broad collaboration aimed at advancing biomedical publishing

MPIP Goals, Structure and 2008 Activities

MPIP Methods

In 2008, we endeavored to gain insights from journal editors and publishers about the publication of pharma-sponsored research in an open, transparent forum.

Organization

- Guided by a Steering Committee of 5 pharma sponsors plus International Society for Medical Publication Professionals (ISMPP)
- Conducted by an independent strategy consulting group (Leerink Swann) to ensure open feedback

Participants

- Targeted editors and publishers of 88 generalist and specialty journals
  - Wide range of therapeutic areas
  - U.S. and E.U. representation
- Successfully recruited over two dozen participants

Format

- Combination of interviews and facilitated group discussions
  - Six roundtable forums to promote open dialogue and brainstorming, in both U.S. and E.U.
  - Supplemental one-on-one interviews
- All results anonymized from sponsors

Initiative participants included senior editors and publishers from a wide range of generalist and specialty journals, therapeutic areas and geographies.

BMJ Group

nature
International weekly journal of science

The American Journal of Cardiology

UROLOGY
OFFICIAL JOURNAL OF THE SOCIÉTÉ INTERNATIONALE D'UROLOGIE

Nephrology Dialysis Transplantation

AIDS

Clinical Infectious Diseases

PAIN

CMAJ
Medical knowledge that matters

AIDS Patient Care and STDs

RESPIRATORY RESEARCH

nature medicine

THE JOURNAL OF CLINICAL PSYCHIATRY

Clinical Cancer Research

Diabetes, Obesity and Metabolism

jth journal of thrombosis and haemostasis

PLoS MEDICINE

WILEY-BLACKWELL
Visit www.blackwellpublishing.com

ENDOCRINE PRACTICE

The Journal of Infectious Diseases

PHARMACOTHERAPY

Contribution of Primary Research

Journal editors and publishers spoke candidly on many issues, and engaged in robust discussions of potential solutions.

Representative Insights from Editors and Publishers

"We need less room for subjective interpretation and more universal guidelines for conflict of interest."

"Some doctors can't write. Professional help can be useful if properly disclosed."

"It's a waste of effort to turn uninteresting results into a full paper."

Key Takeaways

- Research collected individual opinions of editors and publishers
- Aggregate results reflect prevailing views expressed over course of discussion
- Most issues not "black and white"
- Findings do not imply endorsement by journals or sponsors

Editors and publishers identified four areas of interest that present opportunities for collaboration and advancement of common goals.

Publication of Results	For perceived transparency, must all trials be published in traditional journals?	• No – reserve full manuscripts in traditional peer-reviewed journals for highest-impact results • Explore alternate venues for lower-impact results
Publication of Raw Data	Should raw data be made publicly available, and if so, how?	• No consensus on specifics • Journals recognize raw data could aid transparency, but many consider it problematic due to potential misinterpretation and misuse
Finances and Authorship	What more can be done to facilitate transparent disclosure?	• Journals recognize they have not standardized disclosure process • Increased direct, proactive disclosure by pharma would be welcome
Authors' Access to Data	How can pharma enhance the credibility of industry-sponsored studies?	• Ensure that at least one author/investigator has access to full data set

Discussed in detail on following slides

Disclosure of results from all clinical trials would increase editors' perception of pharma's transparency and is a noble goal, but implementation challenges exist.

Rationale for Disclosure of Results of All Trials

- Important to have "clear line of sight" from trial registration to study outcome
- "Less interesting" results may still be scientifically and clinically important

Complicating Factors

- Editorial resource needs
- Competitive intelligence concerns, particularly around early-stage compounds
- Potential lack of appropriate publication venues

There are potential solutions to these issues, however, stemming from editors' recognition that some results are more important than others.

Participants' Views of Need for Detailed Annotation

Low Impact	Medium Impact	High Impact
• Safety (Phase 1) trials	• Clinically relevant negative findings	• Conclusive, important positive results
• Confirmatory trials	• Weakly positive, but suggestive, results	
	• Positive results with less clinical relevance	

Publication of Results – Potential Approaches

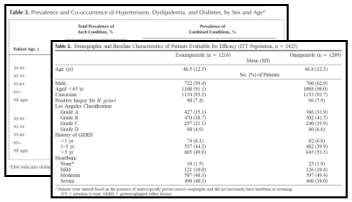
Although editors believe the highest-impact efficacy studies should appear in traditional journals, they suggested several possible venues for other results.

Form of Publication

Impact

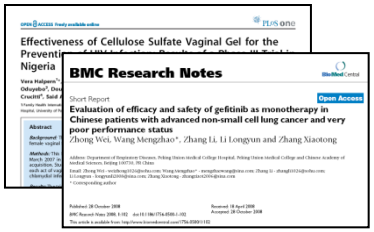
Low Impact

- **Format:** Tables with some description
- Linked to clinicaltrials.gov and/or indexed in PubMed
- Full papers "overkill" for most low-impact work
- **Venues:** Clinicaltrials.gov, published abstracts



Medium Impact

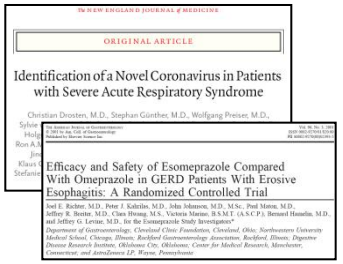
- **Format:** Abbreviated "short reports"; full papers in higher-impact cases
- Indexed in PubMed
- **Venues:** Lower-impact journals, online journals



High Impact

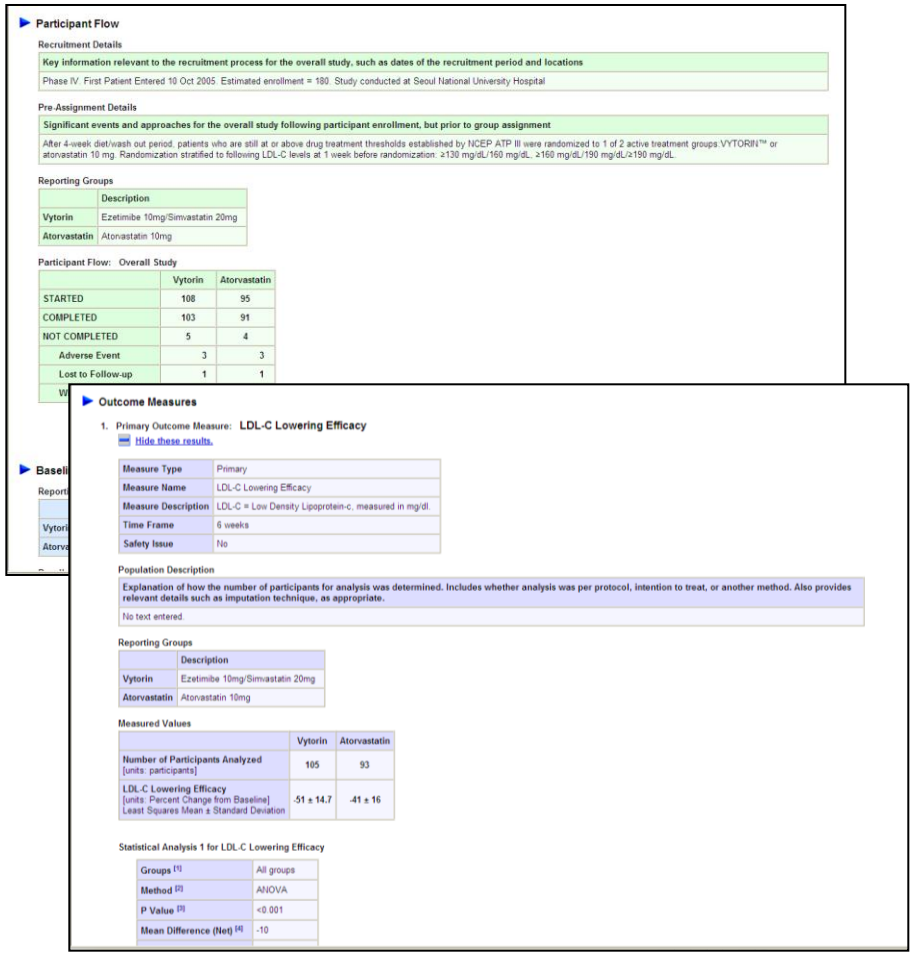
ILLUSTRATIVE

- **Format:** Full manuscripts
- Indexed in PubMed
- **Venues:** Traditional peer-reviewed journals only



Publication of Results – Low Impact Results

For low-impact results, editors support the use of data tables, such as those being incorporated into clinicaltrials.gov in response to the FDAAA.



▶ Participant Flow

Recruitment Details

Key information relevant to the recruitment process for the overall study, such as dates of the recruitment period and locations
Phase IV. First Patient Entered 10 Oct 2005. Estimated enrollment = 180. Study conducted at Seoul National University Hospital

Pre-Assignment Details

Significant events and approaches for the overall study following participant enrollment, but prior to group assignment
After 4-week diet/wash out period, patients who are still at or above drug treatment thresholds established by NCEP ATP III were randomized to 1 of 2 active treatment groups:VYTORIN™ or atorvastatin 10 mg. Randomization stratified to following LDL-C levels at 1 week before randomization: ≥130 mg/dL/160 mg/dL, ≥160 mg/dL/190 mg/dL,≥190 mg/dL

Reporting Groups

	Description
Vytorin	Ezetimibe 10mg/Simvastatin 20mg
Atorvastatin	Atorvastatin 10mg

Participant Flow: Overall Study

	Vytorin	Atorvastatin
STARTED	108	95
COMPLETED	103	91
NOT COMPLETED	5	4
Adverse Event	3	3
Lost to Follow-up	1	1

▶ Outcome Measures

1. Primary Outcome Measure: **LDL-C Lowering Efficacy**

Hide these results.

Measure Type	Primary
Measure Name	LDL-C Lowering Efficacy
Measure Description	LDL-C = Low Density Lipoprotein-c, measured in mg/dl.
Time Frame	6 weeks
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
No text entered.

Reporting Groups

	Description
Vytorin	Ezetimibe 10mg/Simvastatin 20mg
Atorvastatin	Atorvastatin 10mg

Measured Values

	Vytorin	Atorvastatin
Number of Participants Analyzed [units: participants]	105	93
LDL-C Lowering Efficacy [units: Percent Change from Baseline] Least Squares Mean ± Standard Deviation	-51 ± 14.7	-41 ± 16

Statistical Analysis 1 for LDL-C Lowering Efficacy

Groups [1]	All groups
Method [2]	ANOVA
P Value [3]	<0.001
Mean Difference (Net) [4]	-10

Clinicaltrials.gov Results Section

- Information provided about the trial and analysis includes:
  - Inclusion/exclusion criteria
  - Statistical analysis method
  - Summary tables of outcomes
- No introduction or discussion, but allows for links to other sites
- Requires disclosure of PI/sponsor agreements

Publication of Results – Medium Impact Results

For medium-impact results, editors were open to other media besides full-length papers in traditional journals, and cited examples of suitable forums.

"Alternative" Journals

- Indexed in PubMed
- Range of clinical areas
- Typically online only
- Full articles of primary research findings
- Some implement peer review for technical merit only
- Often offset expenses with higher article/page charges
- **Journals:**
  - E.g., PLoS One, BMC journals

Abbreviated Papers

- Indexed in PubMed
- Range of clinical areas
- Online and print
- Short format for research findings with lower impact
- Full peer review for technical merit and impact
- Generally no or modest publication fees
- **Journals:**
  - Available for many generalist and specialty journals

Although venues appear to exist for disseminating a larger volume of results, editors recognized that sponsors' and journals' resources will likely be taxed.

Concerns Regarding Sponsors

- Do sponsors have sufficient resources to support the writing, editing and submission of significantly more articles?

Concerns Regarding Journals

- Journals' editorial, reviewing and publication resources are already strained – how will they deal with even more studies?

- ***Insufficient resources under "business as usual" to deal with predicted increase in volume***
- ***Need more efficiency and streamlining to meet higher demands in timely fashion***

2008 MPIP Steering Committee members

- Kristen Mosdell, Pharm.D., Director, Medical Communications, Scientific Affairs
- Melissa Schreiweis, Ph.D., Senior Manager, Medical Communications

- John Gonzalez, Global Skills Lead – Publications

- Samantha Gothelf, Pharm.D., Director, Global Scientific Publications

- Bernadette Mansi, Scientific Communications Strategy Head, CVM
- Charles Miller, Scientific Communications Strategy Manager, CVM
- David Richards, Scientific Communications Strategy Head, Respiratory

- LaVerne Mooney, Dr.PH, Director, Publications Management, Global Medical

- Larry Hirsch, M.D., Immediate Past President

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MPIP Goals, Structure and 2008 Activities

MPIP Plans for 2009

MPIP Plans for 2009

Possible Activities

As a follow-up to the research phase, we are discussing with the co-sponsors possible future activities to further advance the solution of common problems.

Present *Future*

"MPIP 2.0" – Continue Steering Committee meetings to facilitate future pharma collaborations – ***Ongoing***

Share initiative findings at ISMPP

Discuss opportunities for shared policies across pharma companies in critical areas

Prepare and execute pharma/journal collaborative meeting to develop solutions in key areas

MPIP Plans for 2009

Suggested Formats

During last year's work, editors and publishers suggested that we convene a diverse stakeholder group to explore solutions to key issues.

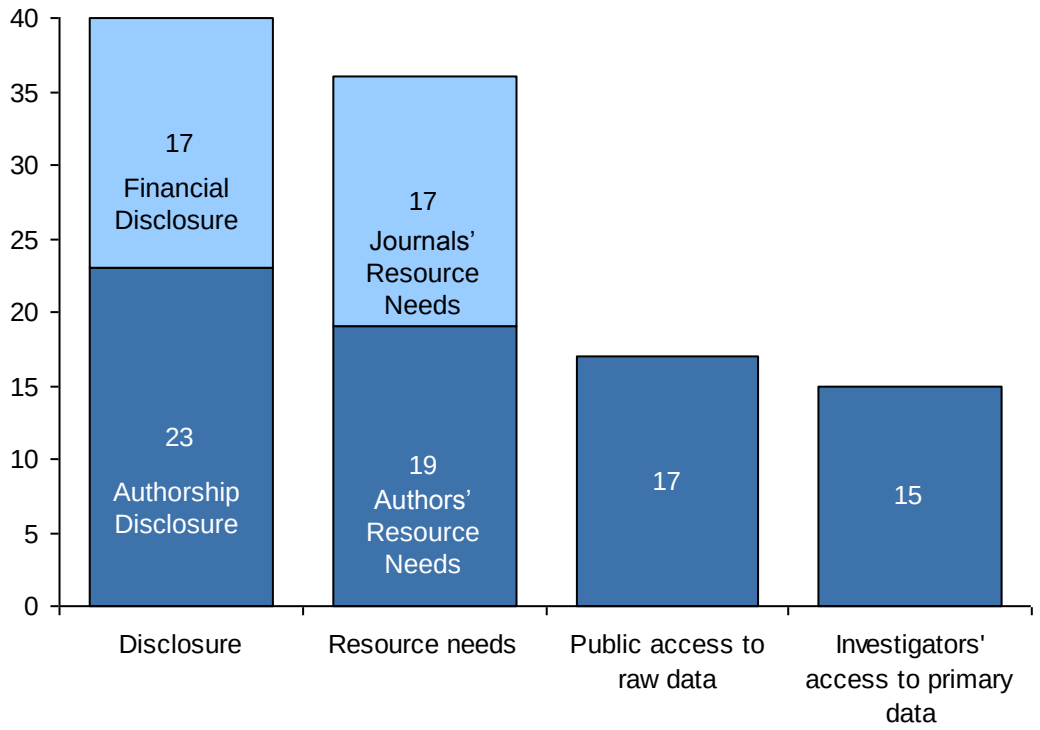
Initiative Format	*Goals and Stakeholders*	*Participants' Perception*
Pharma/Journal One-on-Ones	• Explore journal-specific issues • One editor and one sponsor	 • Some wariness of direct one-on-one interactions
Meetings of Editors and Sponsors	• Jointly explore policy issues • Groups of editors and sponsors	 • Better communication viewed positively
Broad Meetings of Many Stakeholders	• Discuss wide range of publication issues • Editors, sponsors, authors, NIH, etc.	 • Enthusiasm for multi-stakeholder meetings

In a follow-up survey, editors and publishers identified several preferred topics around which to structure such a follow-up event.

Topic Descriptions

- Authorship/financial disclosure
  - Guidelines, trends, unmet needs and potential solutions
- Resource needs for publication
  - Authors/sponsors: e.g., alternate article formats and venues for low-impact or negative studies, assistance for writers, etc.
  - Journals: e.g., financial resources, reviewing resources, etc.
- Public access to raw data
  - Whether raw data should be made available, and if so, how, to whom and under what circumstances
- Investigators' access to primary data
  - Guidelines, trends, unmet needs and potential solutions

Preferred Topics for Follow-Up Event



Note: Survey polled 34 medical editors and publishers; data represent frequency each topic was selected in the top 3 (of 6) most preferred

MPIP Plans for 2009

Follow-Up Event

Among other ideas, several co-sponsors support holding a roundtable with journal and pharma representatives to jointly define submission "best practices".

Objectives

- **Visibly demonstrate sincere commitment on part of pharma to increase trust and transparency with journal editors**
  - Communicate steps already taken by pharma to meet this objective
  - Present data from phase 1 of MPIP Initiative for information and further validation
- **Partner with editors to define article submission "best practices"**
  - Discussion areas could include better journal targeting based on editorial policy, and abbreviated formats and/or template-based "provisional acceptance" for low-interest studies

Logistics

- **Immediately preceding Sixth International Congress on Peer Review and Biomedical Publication (Vancouver; September, 2009) as unaffiliated "satellite" event**

In summary, in 2008 the MPIP aimed to explore editors' and publishers' views of challenges to publishing pharma-sponsored trials, as well as potential solutions.

- **The Medical Publishing Insights and Practices (MPIP) initiative was established to foster increased trust and transparency in the disclosure of pharma-sponsored clinical trial results**
- **To begin to accomplish this goal, five pharma companies and ISMPP came together last year to research key concerns and potential solutions**
- **Through roundtables and interviews with over two dozen leading editors and publishers, we sought to gain insights from journal editors and publishers in an open, transparent forum**

Last year's efforts laid the groundwork for additional potential activities in 2009 aimed at addressing key issues in publishing pharma-sponsored trial results.

- **Our research last year highlighted areas in which editors and publishers saw opportunities for collaborative advancement of common goals by journals and pharma, e.g.,**
  - They support increased data dissemination, and are interested in jointly exploring ways to meet the resource needs of journals and authors/sponsors;
  - They recognize that authorship and financial disclosure rules could benefit from standardization between journals as well as continued proactive disclosure by pharma; and,
  - They support continued efforts to ensure that at least one study author has the ability to access the primary data set for all pharma-sponsored studies

- **By bringing together several pharma companies and ISMPP as co-sponsors and engaging many leading editors and publishers, we laid the groundwork for future potential activities**
  - The MPIP co-sponsors are discussing the possibility of continuing to jointly explore areas of mutual concern and interest, as well as potential collaborative activities
  - Several co-sponsors support hosting an unaffiliated "satellite" event before the Vancouver Peer Review Congress for journal and pharma representatives to discuss submission "best practices"