Disclosures and Conflicts of Interest: Solving the Riddle, Wrapped in a Mystery, Inside an Enigma

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ABSTRACT

Purpose: Confusion exists around the nature and best practices for authors in biomedical fields seeking to disclose conflicts of interest (COIs) and other information that can produce bias. Guidelines often provide principles for action and to avoid granularity that can limit their general usefulness. Journal editors must also interpret various guidelines to produce and enhance their own disclosure and COI policies. We discussion COIs and present heuristics that can enhance disclosure practices by individual authors and inform policy and practice among medical journal editors.

Methods: The authors reviewed the biomedical literature and drew on professional and academic experience to develop examples and a suggested matrix for decision making.

Findings: Most COI commentary centers on financial relationships. Disagreement still exists about the nature and impact of various forms of COI, making critical reasoning essential when making and interpreting disclosures. Journal editors, authors, critics, and other experts express varying opinions about best practices regarding COIs. Policy decisions should be balanced and reasonable. Narrative context may help readers understand the meaning and relevance of disclosures and COIs.

Implications: A balance of personal responsibility and critical thinking can enhance disclosure practices as well as confidence in the medical literature. Using a heuristic to think through possible areas of conflict can help authors provide more complete disclosure information. Providing narrative context can ease the burden of peer reviewers, editors, and readers trying to understand disclosures. (*Clin Ther.* 2019;41:2643–2655) © 2019 Elsevier Inc. All rights reserved.

Keywords: conflict of interest, disclosure, ethics, journal policies, transparency.

"What we've got here is a failure to communicate."[1]

- *Cool Hand Luke*, 1967

"Even in the absence of evidence that research quality has dramatically suffered, conflicts of interest can create the appearance of impropriety."[2]

- A 2008 Hastings Center Report on Conflicts of Interest

INTRODUCTION

Attendees of the 2017 International Publication Planning Association meeting laughed when one of the authors prefaced a comment by disclosing a financial relationship in the amount of $59.96.[3] The disclosure was meant to be tongue-in-cheek, but it also raised a more serious concern: at what point does the reporting of financial relationships distract from matters of substance? Remarks at the 2019 International Society of Medical Publications Professionals (ISMPP) plenary session on conflicts of interest (COIs) revealed that these questions still hold interest.[4,5]

COI is a current hot topic both in biomedicine and the press, resulting, as Johnston[2] noted in a Hastings Center Report, from increasingly blurred boundaries between academic inquiry and corporate sponsorship. A 2006 study revealed that more journals had COI

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policies than authorship policies.[6] In recent years, these questions have become more pressing.[7–9] A notable case, José Baselga, reportedly failed to disclose millions of dollars in payments from commercial entities in dozens of research articles in top tier biomedical publications.[10,11] The news circulated widely in the press and social media, opening questions not simply about one person's practice in filling out disclosure forms but also about the overall quality and integrity of cancer research and medical journals worldwide. Baselga revisited his previous disclosure practices, apologized,[11,12] and resigned from his post at Memorial Sloane Kettering, but somehow that did not seem to be quite enough. Something, the public demanded, *had to be done,* which supports the International Committee of Medical Journal Editors (ICMJE) position that perceptions of COIs are as important to consider as actual conflicts.[8] If the recent discussions at the 2019 ISMPP meeting are any indication,[4,5] the current sensibility is to hold authors directly accountable for their own disclosures; however, the question remains as to how authors can better understand what is expected of them.

Studies in the early 2000s indicated both troubling effects of corporate sponsorship on academic research quality and the need for such collaborations,[2,6,8] a sentiment echoed by Harvard's chief of medicine.[11] The necessary relationship between industry, government, and academia in biomedical research creates a double bind: no one really knows whom to trust, what to disclose, or how—including the editors of the world's top journals. In May 2017, the *Journal of the American Medical Association* (*JAMA*) published 23 expert viewpoints on COIs, intended to shed light on the ongoing public debate about defining potential sources of bias.[7] As Fontanarosa and Bauchner[13] detail, the key concern is to identify areas in which a person's professional judgement might be influenced by some secondary interest; therefore, the *JAMA* family of journals, like many other biomedical journals, require the disclosure of "relevant" COI information. This single word highlights a key problem: the idiosyncratic nature of interpreting disclosure, reporting, and conflict and the implicit recognition that at some point the level of disclosure will become susceptible to ridicule. How does one define relevance, given that questions about COIs persist even when they are clearly not relevant to the quality or conduct of research.[2,8,9] Ultimately, what we have, in the words that Cool Hand Luke co-opts from his captor, "is a failure to communicate."[1] In the sections that follow, we describe some of the key concepts at stake in COI disclosures and suggest a scaled model for reporting to help authors and others negotiate this difficult territory.

A CRITICAL DISJUNCTION IN UNDERSTANDING

A critical question is that COIs are perceived as creating problems even when they do not adversely affect research quality, making suspicion the key underpinning of public outrage.[2,8,9,14,15] Any possibility that a COI exists can impugn researchers' integrity and morality. The notion of relevance is lost in such conversations, despite the importance of the relationship between interests and their impacts on one another.[16] Researchers, reasonably enough, tend to distinguish financial relationships, research bias, and outright dishonesty, relying on their critical reasoning abilities, and those of their colleagues, regulators, patients, and peers to tease out the differences between receiving a research grant, working for hire at a corporate entity, or collaborating on research with biotech or manufacturers. They further expect others to understand the difference between receiving funding to compensate a statistician for his or her time and being paid $25,000 to lend a name to a ghostwritten paper commissioned by an advertising executive.[15,17,18] Some of these activities create an obvious bias or represent inappropriate exchanges between sponsors and researchers or prescribers, whereas others create more nuanced relationships and dependencies that are not necessarily suspect.[2,8,9,15–18] Nevertheless, differences remain in perception of COIs among those who collaborate with industry and those who do not,[19–21] and it may be difficult for laypersons to identify exactly which of these gifts creates the most unconscious or conscious bias.[8,17,18,22]

As a broad body of biomedical literature reveals, many authors believe that declaring a payment means no conflicts exist, whereas others fear that disclosures will undermine faith in their scientific judgement.[2,4–9,12–29] In addition, in some cultures, disclosing relationships exposes persons to accusations of corruption, resulting in a fear to disclose. Others

associate the word "conflict" with bias and therefore may view results based on established empirical research methods as inherently trustworthy and immune to the influence of financial support or personal relationships.[2,4,5] On the other end of the spectrum, peer reviewers may border on paranoia, requesting information far in excess of that required by journal editors or recommended by respected editorial groups such as the Committee on Publication Ethics.[8,29]

One of the authors (L.C.) was recently chided for a vague disclosure of pharmaceutical company relationships which read: "No external funding or writing assistance was used in the creation of this review. … In the past 12 months, consultant: Acadia, Alkermes, Allergan, Intra-Cellular Therapeutics, Janssen, Lundbeck, Merck, Neurocrine, Noven, Otsuka, Pfizer, Shire, Sunovion, Takeda, Teva, Vanda; speaker: Acadia, Alkermes, Allergan, Janssen, Lundbeck, Merck, Neurocrine, Otsuka, Pfizer, Shire, Sunovion, Takeda, Teva; stocks (small number of shares of common stock): Bristol-Myers Squibb, Eli Lilly, J & J, Merck, Pfizer purchased >10 years ago; royalties: Wiley (Editor-in-Chief, *International Journal of Clinical Practice*), UpToDate (reviewer), Springer Healthcare (book)." At first glance, it would be difficult to say what else L.C. could have added, because this list of disclosures is extensive and may be difficult to decipher. The peer reviewer requested monetary amounts for each relationship, granular information that in the United States is readily available (and regularly updated) online at Open Payments to identify payments from pharmaceutical companies to physicians. It is worthy of note that dollar amounts do not help differentiate which of these revelations are, in fact, the most relevant to the subject matter being discussed.

Additional problems can arise because of seemingly contradictory information. Reviews may be authored by prominent experts with the aid of medical writers paid by pharmaceutical companies with a strong commercial interest in the subject matter.[4,11,22] These sponsors often also pay open access fees. Yet, although such funding is usually acknowledged, in accordance with best practice,[8,22] the author might also declare no COIs. In a further exercise in contradiction, the author may then disclose consulting relationships with the sponsors of the published article. An anonymized example adapted from the recent ISMPP COI panel[4] appears in Box 1, which details the acknowledgements and author disclosures of Dr. Jones, the sole author of a review paper about a product made by BigPharmaUSA and also distributed and manufactured by MediumPharmaEU. The author declares no COI, whether "relevant" or not, but consults for the manufacturers that funded the medical writing support. Certain things remain unclear. Did the journal standards describe relevance? Did the author merely feel unbiassed? Did the author consult for this sponsor pro bono? The disclosures provide no context.

Although it is agreed that transparency of disclosures and policies increases confidence in the research, the application of this transparency remains moot.[24,28] No interpretation of COI and appropriate disclosure is universal, although Bero[25] notes the ubiquity of bias in research, indicating that the entire discussion may remain at loggerheads indefinitely. A key issue is that the lack of clarity inherent in such discussions emanates from conflicting beliefs and definitions. Even Fontanarosa and Bauchner[13] refer to the need for "judgement" because the nature of COIs requires an evaluation of the risks and benefits inherent in research relationships, sponsorship, and funding.[13] An inherent lack of clarity and need for critical thinking stands at the center of disclosure and COI, just as the need for industry–academic ties undercuts the idealistic perspective that a location of pure research, such as that Bero[25] calls for, may well be impossible. As Basulaiman et al[23] observe, the best course of action may be rigorous self-accountability—ensuring that our own disclosures are complete and correct. Lo and Field[16] similarly recommend considering proportionality, severity, and the distinction between an appearance of conflict and an actual conflict. We offer some explanations of the inherent problems in these discussions before offering a matrix for disclosure and reporting.

DEFINING THE TERMS

Failures to communicate effectively about COIs derives only partly from terminology because personal feelings also affect the practical aspects of disclosure.[30] Associations of bias, conflict, the terminology of conflict, interests, and disclosures and integrity vary between individual authors, editors, and members of the public.[2,9,27,28] Thus, researchers, anticipating faulty perception of COIs, might adjust their

Box 1
Contradictory disclosures.

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practices to compensate for expected misinterpretations of their actual relationships (see McCoy and Emanuel[26]).

Fineberg[27] suggests that the standard applied in COI disclosure and interpretation should depend on what a reasonable person might believe would influence medical thinking. The reasonable person standard should be supplemented, especially insofar as the general public is concerned, on what has been defined as a normative interpretation of terminology in rhetorical studies of medical language. Thus, researchers, sponsors, authors, and editors should all consider normative definitions of terminology as well as the nature of COIs that might unduly influence medical thinking. In other words, researchers and editors must adopt commonly understood terminology and usage rather than expecting the general public to read up on the nuances of uses for specific terms in particular contexts. For example, it would be unreasonable to expect a lay reader to discern differences between various definitions of what constitutes a relevant COI, even if journals or other venues define the term at each instance (Table).

Interests are commonly defined in the biomedical literature as either primary or the main goal of professional activities, such as promoting the health and welfare of patients.[16] As described by Fineberg,[27]

Table. Terms and brief definitions.

Term	Brief Definition
Interest	Investment in a specific outcome such that a party will benefit or be rewarded for one outcome over another. Examples: a researcher will have an interest in the success or failure of a study; an employee will receive a salary.
Conflict of interest (COI)	When a party has an interest inconsistent with benefits to others or the intended purpose of a specific activity. COIs include any situation in which the concerns or aims of two different parties are incompatible, or a situation in which a person is in a position to derive personal benefit from actions or decisions made in their official capacity. Examples: a researcher will benefit financially or professionally by exaggerating the significance of a research study or falsifying data; a peer reviewer will benefit personally by undermining the work of a direct rival; a physician who is deeply in debt and could receive financial incentives from manufacturers for prescribing one product over another may be tempted to deviate from best medical practice.
Competing interest	When a party has different interests that may influence its opinions or benefits; such interests have a strong potential to create a COI or other type of bias. Example: employees of research entities or manufacturers may be worried both about study success and the potential impact of failure on their jobs or annual

Table. (*Continued*)

Term	Brief Definition
	bonuses, even though they may not be authorized to make decisions that directly affect the overall study.
Confluent interests	Interests that work together or reinforce each other. Examples: a researcher who gains scientific credibility as the result of successful studies and publications; an employee of a large company may have an interest in the success of a study both because it furthers scientific endeavor and because it contributes to the scientific credibility of their institutions.
Potential COI	A factor that may become a COI for a specific party but has not yet done so (and may never do so) or a factor that benefits an institution but not an individual person within that institution. Example: a researcher whose institution receives funding for a study from a corporate entity that is used solely for research conduct; holding a patent on a process to produce a chemical entity; study success for a new product.

Adapted.[2,6–9,12–30]

primary goals should be disinterested or not focused on other outcomes that may affect the health care provider or prescriber. Secondary interests, however, include such things as financial gain, professional relationships, and professional standing; therefore, they are often not disinterested. It remains open to interpretation whether these interests are necessarily relevant to specific professional activities and are therefore capable of creating a COI.

COIs are generally identified when a secondary interest, such as the exchange of large sums of money,[2,9,16,17,21] might be expected to influence the primary interest at stake. Other terminology such as competing interests or confluence of interest has been suggested to address the inherent necessity for collaborations between academia, industry, and government entities.[2,14,16,18] A further complication arises in terminology such as potential COIs, which can be found on the ICMJE COI disclosure form and its instructions.[28] As McCoy and Emanuel[26] indicate, such terminology is confusing and adds to the potential for reflexive or conscious corrections of perception rather than honest, transparent reporting, as recommended by other experts.[28] For example, even though employees of a small company may have a COI when testing their only product, this does not mean that they will behave with a lack of personal or professional integrity.[16] Varying, but still similar-sounding, terminology may also complicate or undermine the reasonable person standard by making it difficult for laypersons to decipher the relevance or significance of different terms.

INTEGRITY, HONESTY, BIAS

An explicit argument in almost all discussions of COIs is the idea that financial entanglements create bias that might be sufficient to impair investigator's judgement. At stake in these discussions is the notion that potentially impaired judgement leads to an abnegation of the moral and ethical responsibilities of medicine, or worse, a vitiated personal integrity that leads to intentional dishonesty for the sake of personal gain. Because these arguments are rarely made explicit, it is difficult to address the function of faulty logic in equating a financial relationship with intentional lying. An interesting fallback position among the general public and academic physicians is that there exists a conflict-free group of educated experts who are capable of making assessments of biomedical research.[9–11,25] Generally, however, this absence of conflict is construed as financial and, as several experts have noted,[2,13,27,30] bias can arise from many different sources: personal relationships, loyalty to one's school, national identity, religion, or educational background. Thus, it is impossible to truly erase secondary and personal interests from the conduct or reporting of biomedical research. Indeed, professional and personal rivalries can plague peer review of biomedical publications if the editor is unaware of the backstory. Few guidelines mention these relationships, and even tools such as Elsevier's

Competing Interests Fact Sheets provide only high-level guidance for teasing out these relationships.[30]

Fortunately, scientific research, including biomedical research, is designed to be self-correcting: studies are considered to be increasingly credible depending on the rigor, validity, and reproducibility of their methods; their sample size and power; and the ability to mask treatment identities and other identifiers at appropriate times. It has also been noted that opinion pieces, viewpoints, and non-systematic reviews are inherently biased, for the good reason that they are intended to present opinions and personal interpretations—in other words, bias is part of their value. Therefore, it has been suggested that researchers and the public rely on measures of credibility, such as those used in evidence-based medicine, as a guide to the appropriate uses of different types within the medical literature. Of course, such a recommendation requires not only a measure of credibility but also the exercise of critical reasoning in interpreting it. If we believe that a reasonable person standard is essential to solving the problem of COIs,[27] then such measures are similarly important.

DISINTEREST AND THE RIGHT TO HEALTH

Unfortunately, the cognitive dissonance that currently informs discussions of COIs is not an isolated circumstance within the public discussion of biomedicine. Underpinning the notion that a pure area of disinterested research exists is a series of powerful, yet largely unspoken beliefs in a right to health. Sociologist Deborah Lupton[31] has described a common cultural tendency to believe in a the nearly godlike power of the medical profession to ward off illness before it begins as a result of the rise of vaccination in developed countries. Coincident with this veneration of the medical field is the unfortunate tendency to demonize any failure to deliver on perfect, risk-free health untainted by personal or financial interest. In other words, the public perception of medicine is simultaneously a force of benevolent selflessness with powers bordering on the mystical and a seething pool of malevolence bent on exploiting the unsuspecting for personal gain.

Although these dueling ideas work well in Hollywood films, they impair the exercise and even the development of a reasonable person standard as regards COIs. A critical feature of both sides of the benevolent selflessness/seething malevolence model is the passivity of patients and readers: all of the activity is left to medical practitioners and researchers, with the occasional intervention of ghostwriters. A reasonable person standard does require that patients, and other readers, weigh and consider various risks, including the potential for harm in the omission, whether accidental or not, of certain financial relationships—in other words, such a standard might call on individuals to consider whether they, themselves, might behave in such a way in similar circumstances. A reasonable person standard would also require an acknowledgment that personal interpretations of the relevance of financial relationships are themselves often reasonable. Finally, such a standard mirrors the notion that locating actual problematic practices, rather than merely the possibility that such practices could exist, is the rational approach.

Ultimately, the suggestion to be as realistic as possible about the goodwill and professional practice of authors and researchers could go a long way in ameliorating the problem of overreaction to COIs. Basulaiman et al,[23] for example, suggest forbearance toward others when interpreting their disclosure statements and reading them as intended to be as helpful and complete as possible, rather than immediately seeking to find fault. This, of course, is quite a tall order. Consider, for example, the fact that all of the most important guidelines and statements about research integrity and medical ethics are themselves a reaction to horrible atrocities, ongoing problematic activities, or new troublesome discoveries of unethical practices as we can see with core documents such as the Nuremberg Code, the Declaration of Helsinki, or even the ICMJE Recommendations. Thus, we offer some pragmatic advice designed to augment existing rules and guidelines.

EXISTING GUIDELINES: ICMJE AND GOOD PUBLICATION PRACTICE 3

The most commonly accepted guidelines for reporting COIs are those designed by the ICMJE. The major categories in this COI disclosure are the following. (1) COIs related to the work under consideration: by exercising a reasonable person standard, it is not illogical that many authors consider the present work to include only the materials in a specific study. (2)

Relevant COIs in the broader medical field: the ICMJE addresses the possibility that other relationships and endeavors in biomedicine may also influence the author's present work. This section includes all payments to the author or their institutions. (3) Patents and intellectual property, including royalty payments: this category is relatively straightforward. (4) Any other potential COI that readers could perceive to have influenced the present work: this category, as indicated in many of the essays in the 2017 JAMA special issue and others, leaves open the question of relevance.

The ICMJE disclosure form specifies relationships within the preceding 36 months. One might also comment that the disclosure of L.C. follows this general format, presenting each of the elements outlined by the ICMJE, in order, and yet was still criticized by peer reviewers.

It is worthy of note that the language used in the ICMJE COI reporting form leaves open many of the questions discussed in the 2017 JAMA special issue on COIs. Yet the ICMJE usage does not appear to be intended to invite semantic parsing or terminology. Instead, it uses language about potential and perception that specifically invites authors to consider whether a reader would reasonably view certain relationships as COIs. In other words, the ICMJE might be seen as already using a reasonable person standard. Ongoing questions about COIs might therefore benefit from more granular advice. One approach might be toward a general category of disclosures rather than COI, as suggested by the Good Publication Practice 3 (GPP3) guidelines created by ISMPP.[22] Essentially, this is a shift in terminology intended to provide a more useful conceptual framework for readers. Despite the thoughtful discussion within GPP3, its advice remains high level and emphasizes the absence of universal standards; hence, further clarification may be helpful.

Publishers also provide guidance for authors in preparing their disclosure statements; however, these may be overlooked against an array or different topics in publication ethics. For example, Elsevier provides brief guidance about topics such as avoiding plagiarism; data access and retention; multiple, redundant, or concurrent publications; acknowledgements; disclosures; handling errors in published works; accuracy and reporting standards; protection of human subjects and ethical treatment of animals. The Competing Interests Fact Sheet also provides examples of COIs that may result from personal relationships, professional competition, or even what they term "intellectual passion."[30] The advice given in the context of the Fact Sheet remains high level while enjoining authors to be specific and complete in these disclosures.[30]

APPROACHES TO DISCLOSURE CATEGORIES FOR AUTHORS

The ICMJE requests information to cover several domains: the present work, the wider medical field, intellectual property, and any other so-called relevant COIs. Thus, it might be helpful to provide some thinking points to help guide authors seeking to assemble this information. In developing these points, we consulted different contributorship guides, which provide a fairly detailed list of categories of colleagues who could be credited with their work on a primary clinical study.[8,23,29,30]

Some General Considerations

Various Sunshine Acts require that payments to physicians be reported in publicly accessible databases, such as the US Open Payments web site. As noted, these sites provide data that is both global and granular as well as regularly updated. Similarly, many academic centers, hospital systems, and government agencies also provide publicly accessible information about monies received from various sources. Authors might consider including links to such information in the acknowledgments of their papers. Obviously, publicly accessible databases are not available to account for the work of all authors of papers in biomedical journals; however, when such databases exist, it would seem logical to use them as a reference, especially because such databases, unlike the disclosures in a given paper, are kept up to date. Academic and nonphysician authors might use services such as Research Gate or Academia.edu to keep their current financial and other disclosures up to date.

Disclosures Relevant to the Work Being Reported

For clinical trials and meta-analyses of clinical trials or other studies that collect and analyze data, such as health economics and outcomes research, at a minimum consider (1) funding for study conduct, including laboratory tests, overheads, or salaries for

people who work for the author; (2) funding for the paper, including the open access fee, page charges, fees for color figures; (3) salary or consulting fees paid directly to the author; (4) travel expenses for investigator or other meetings (if travel was to a meeting to present data, report source of funding to print a poster and/or handouts); (5) financial relationships regarding any investigational materials or comparator products used in any study reported, including rescue medicines and delivery devices; and (6) writing support, including medical writers or publications professionals who provided support (including submission or handling peer review comments), mentioned by name as well as the source of funding for their work.

For reviews (including systematic literature reviews)/ editorials/opinion pieces, consider the items mentioned above plus the following: (1) for reviews on general subject matter areas that do not mention specific products: relationships with corporate and other entities that have supported the author's research in that therapeutic or scientific area, (2) for reviews funded by a sponsor: whether the author requested support or the sponsor requested the author's participation and offered support as well as any other connection with the manufacturer of any products mentioned in the paper, (3) payments to the author for his or her time, and (4) any financial interests related to individual studies or products discussed in the paper.

For consensus statements and treatment guidelines, consider the items mentioned above plus the following: (1) history of leadership positions in the professional area or related medical societies and (2) participation in review boards for granting bodies.

Disclosures That are Relevant to the Individual Within the Broader Medical Field

Authors should consider the following in addition to the relevant categories that apply to the given work: (1) employment, including previous employment or education, by the sponsoring institution or any of its competitors; (2) participation in additional clinical trials of the product and/or comparators in the present work (following the guidelines above); (3) participation in clinical trials of other related products (ie, within in a similar therapeutic area or similar types of products); (4) authorship of additional opinion pieces, reviews, or viewpoints in the general therapeutic area or on products with a similar mechanism of action (if not already cited in the present work); (5) stock ownership; (6) additional exchanges that qualify as a transfer of value under applicable regulations; (7) participation on advisory boards or grant selection committees; (8) speaker fees; (9) delivering continuing medical education; (10) editorial boards (specifying whether compensated); (11) board memberships by the sponsoring organization or any competitors; and (12) leadership positions in any other setting that may generate revenue.

Intellectual Property

Authors should consider the following in addition to the relevant categories that apply to the given work: (1) patents, licenses, copyrights on products; (2) publications (such as books) that generate royalties; and (3) blogs or other online publications that generate revenue.

Additional Information

Additional relevant information would include (1) editorial boards, peer review relationships; (2) editing a journal, blog, or book series; (3) personal relationships with patent holders, government employees with responsibility for public health decisions, or company officers; (4) professional society positions that generate revenue or exert influence on a therapy area or professional field; and (5) if serving or having served as an expert witness in legal proceedings regarding cases about the disease or treatment in question, who they worked for.

MAKING DISCLOSURES MEANINGFUL

We opened this article with examples of disclosures that appeared vague or unclear. A reasonable person standard might dictate that it is necessary to understand the context for specific disclosures. One reason for this lack of clarity may have been an absence of narrative information to help make sense of the material being disclosed. Thus, we also suggest that journals and authors support a more writerly approach to disclosures. With the use of L.C.'s disclosure as an example, one could envision a section that reads:

Funding for present paper. The author received external funding or writing assistance for the present paper.
Consulting. Within the past 12 months, the author consulted with the following corporations on [direct topic of paper]: [list]; with the following companies on related topics: [list, formatted as Company (topic)]; and with the following companies on unrelated topics: [list, formatted as Company (topic)].
Stock ownership. In [year] author purchased small numbers of shares of common stock in the following companies that investigate or have an interest in [direct topic of paper]: [list]; and the following companies that have an interest in related topics: [list, formatted as Company (topic)].
Royalties. The author receives royalties as the Editor-in Chief of (Journal) and a reviewer for UpToDate; in these roles, the author expresses independent opinions on a variety of topics [specify relationship to present paper]. The author also receives royalties on a book [Title of book].

The differences between this suggestion and the original example highlight questions of relevance for the reader, grounding the disclosure against the most clearly related financial and other interests as well as the least related. In other words, this new example provides an answer to the reasonable question of how the disclosure is related to the work. Authors might adjust the headings as needed, for example, to include relevant personal relationships as described.[30]

If we were to adapt the second example, a more helpful disclosure might also be developed (Box 2). This disclosure contains generally the same information, but, by providing a clearer framework for the reader, it also imparts better information about the relationship of the author to the funding source for the paper as well as the consulting company to the sponsor. The suggested disclosure also provides additional, helpful information about the qualifications of the author to produce a review paper.

THE ROLE OF PUBLICATIONS PROFESSIONALS

Both authors of this commentary are active members of ISMPP. As mentioned earlier, the general opinion among many ISMPP members is that author disclosures are the responsibility of individual authors.[4,5] We agree; however, a few words about the conditions of publishing in collaborations between employees of corporate entities and academics are warranted.

Often, publishing with industry partners is driven by deadlines that track with specific events, such as a product launch date, the release of new treatment guidelines for a specific medical condition, or the update of vaccine schedules. This circumstance is reasonable, especially because the timely disclosure of information in published forms is consistent with the principles outlined in the Declaration of Helsinki and therefore supports transparency and medical ethics. To meet these goals, manufacturers often hire medical writers and publication professionals.[22] It is a natural impulse for authors to rely on such professionals for what might be perceived as more bureaucratic elements of publications, such as proofreading, overseeing quality control checks, journal submission, reminders about the nuances of journal requirements, or tracking author comments. Unfortunately, it may become all too easy for authors to assume that financial and other disclosures fall into this general purview. Sadly, this is not the case.

Although publication and medical writing experts, especially those who work full time for specific sponsors, may have access to certain types of financial information, they will never be able to aver or guarantee the full disclosure of financial and other potential COIs for other colleagues. Yet, although we enjoin authors to pay more attention to their own disclosures, we also believe that the publications process could provide added support. For example, in keeping with GPP3, it is routine in many companies to begin all publications with a launch meeting and to ask authors to agree to follow ICMJE authorship guidelines.[22] Adding information about financial disclosures to the basic author responsibilities at manuscript launch could go a long way toward avoiding accidental omissions. Assigning a disclosure champion, preferably the lead author or the chair of the publication steering committee (should one exist), would also help emphasize the importance of these disclosures.

ACTIONS FOR EDITORS

Despite the best efforts of editors, peer reviewers, and authors, sometimes a relevant COI is not disclosed.

Box 2
More helpful disclosures.

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The author has served as an expert witness for 3 trials on behalf of MiniPharmaLatAm and has published several opinion pieces on the topic of the present manuscript.

This circumstance may arise from misunderstandings, honest error, other miscommunications, or may be an intentional effort to mask the real relationship between an author and a funding source. The latter is a serious breach of medical ethics and should be addressed appropriately.

The Committee on Publication Ethics has published guidelines for handling reviewer suspicions that an undisclosed COI exists as well as guidance for handling post-publication complaints.[29,32] The general approach to reviewer suspicions, we believe, should be used for any straightforward post-publication questions about COIs. The Committee on Publication Ethics process for clarifying COI statements before publication includes asking the author about reviewer questions, providing a reminder of the journal policy, and publishing any needed correctives.[32] After publication, this may involve publishing an update to an existing paper, which would be reasonable in the case of an accidental or minor omission. Examples of minor omission might include (1) one author provided disclosures for 12 months, whereas all the other authors gave 36 months of information; (2) a financial disclosure is found to have a numerical error; (3) the name of a funding body changed between the submission and publication; (4) after being apprised of the failed disclosure, the lead author finds a cut and paste error in the final revision that deleted information included in the initial submission; and (5) an author's affiliations changed during the period between acceptance and page proofs and the lead author forgot to include the new information.

It may be possible that the editor believes that the failure to disclose certain relationships undermines the integrity of the reported research sufficiently to warrant a retraction or an expression of concern. In our opinion, such action should not be taken until all authors on the paper have had an opportunity to address any questions that have arisen. Editors must carefully consider the degree to which all authors were aware of this failed disclosure or supported it. In such cases, it would be important to understand the potential COIs of all authors and their relevance to research integrity.

OTHER POTENTIAL SOURCES FOR MISCHIEF

Although an author's reasonable disclosure may help the public understand any kind of bias that may have (intentionally or unintentionally) influenced the research and/or manuscript, the public is generally completely unaware of any reviewer (or editor) conflicts, which could similarly influence what is, and what is not, accepted for publication. There may be also different thresholds for "famous" people compared with those who are not well known. A

complete discussion of this is beyond the scope of this commentary; however, we do recommend that editors consider requesting disclosures from peer reviewers, as is already the practice at some journals.

CONCLUSIONS

We believe that the concept of disclosure should replace the terminology of COI, competing interest, and confluent interests. As an example, this step is being taken with the journal you are currently reading, as eloquently expressed in an Editor-in-Chief's Advisory.[33] Disclosure has the benefit of being non-blaming and of avoiding value-laden judgements about bias. However, disclosures without meaning are useless to authors, editors, and readers. Therefore, we believe that authors and editors should endeavor to support a culture of transparency and honesty that is rendered meaningful by adequate context.

All readers of the biomedical literature should try to understand that the people who engage in research are humans, at risk for honest mistakes, but generally and overall doing their best to improve human health. As humans, researchers have relationships, opinions, and flaws. Although it is reasonable to expect honesty and transparency from the people undertaking biomedical studies and authorship, it is unreasonable to seek perfection and a complete lack of error. Thus, although we support full disclosure of financial relationships and other potential COIs, we remind the reader that additional forms of bias may exist. These might include personal relationships, educational affiliations, national allegiances, or political views, none of which should rightly be collected and reported under current standards. Finally, we believe that, although disclosures are vital, they are not sufficient to render research complete or reliable and that we must depend on the inherent skepticism of scientific inquiry to continually retest our assumptions to ensure that medical knowledge continues to improve.

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No funding was provided for the current paper, which was invited by the editor-in-chief based on his professional and personal regard for LC. All opinions are those of the authors and not their institutions. Neither author expects to gain financially by the publication of this paper, either directly or indirectly.

In the 12 months prior to submitting this manuscript, LC was a consultant to the following companies: Acadia, Alkermes, Allergan, Intra-Cellular Therapies, Eisai, Impel, Janssen, Lundbeck, Merck, Neurocrine, Noven, Osmotica, Otsuka, Pfizer, Shire, Sunovion, Takeda, Teva, Vanda; served as a speaker for: Acadia, Alkermes, Allergan, Janssen, Lundbeck, Merck, Neurocrine, Otsuka, Pfizer, Shire, Sunovion, Takeda, Teva; owned a small number of shares of common stock purchased more than ten years previously in the following: Bristol-Myers Squibb, Eli Lilly, J & J, Merck, Pfizer; received royalties from the following: Wiley (Editor-in-Chief, International Journal of Clinical Practice), UpToDate (reviewer), Springer Healthcare (book).

In the 12 months prior to submitting this manuscript, LD was a paid consultant through Synchrogenix. LD receives royalties from McFarland and the Regulatory Affairs Professional Society from edited collections on superheroes and regulatory documentation, respectively. LD is also a co-PI on an NSF grant and senior staff on another NSF grant through Hofstra University. Despite not having been a full-time employee of any corporate entity for several years, LD retains fond feelings for former employers, including Merck and Co., Inc., Sanofi Pasteur, EMD Serono, and Novartis Vaccines.

Both authors are members of ISMPP and frequent speakers at TIPPA. LD has been a member of the ISMPP Ethics committee (or Ethics and Standards committee) since 2010. Some of the work for this paper was completed while at the 2019 Harris Manchester Summer Research Institute at Oxford University.

CONTRIBUTIONS

ICMJE authorship roles: Both authors participated in the design, writing, and critical review of the paper. Both authors approve of the final draft and agree to take public responsibility for the work.

CREDIT ROLES

LC led the initial conceptualization and information curation of the manuscript, wrote the first draft and provided critical review of subsequent drafts.

LD reviewed the curated information, added resources, expanded the initial draft, and incorporated critical comments from LC.

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