NHLBI’s Conflict of Interest: Why We Need the Data Quality Act

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In 2001 Congress passed the Information Quality Act with little fanfare and on October 1, 2002, that legislation became law. In lengthy coverage on that date, the Washington Post intimated that with sparse recognition outside the Beltway, business as usual for many federal agencies changed overnight. The intent of Congress for this legislation is to ensure that data generated by the government and then used in setting policies, communicating information to citizens, and creating new federal regulations are based on a fair, unbiased analysis and interpretation of the research underlying an agency’s position. In other words, the government must meet the same standards of full disclosure of scientific information that the private sector is held to by many of these same governmental bodies.

The legal underpinnings are simple and are difficult to challenge on any logical basis. The Data Quality Act, as it has become known, requires the relevant governmental agency to make available in a full, comprehensible, and transparent fashion all data cited in support of an agency’s action that was generated by publicly funded research. Any party that has a substantial interest in the issue that the agency is attempting to influence can request access to this information.

In a very real sense, Congress was acknowledging a critical shortcoming in the oversight of the use of scientific data by federal agencies—the presence of inherent conflicts of interest in funding research that is then used to influence society without independent validation of the quality and accuracy of the data and of its interpretation and presentation. In our field of medical science, it is important to understand the appropriateness of this legislation. No cardiovascular researcher would support the release of a new therapeutic agent or device for use in patients without the independent review of all available data by the Food and Drug Administration (FDA). We are fortunate to have not only the FDA but the FTC as well to review and to approve the communication of factual information used by companies to market their medical products. The Data Quality Act simply mandates that federal agencies be held to the same standards applied to private industry in placing into the public domain the data supporting their claims—a concept that is difficult to argue against.

The Data Quality Act has recently been employed to challenge the inappropriate use of undisclosed data from the National Heart Lung and Blood Institute (NHLBI)—funded Dietary Approaches to Stop Hypertension (DASH)-Sodium Trial. The original publication of this trial’s results in the New England Journal of Medicine in 2001, a subgroup analysis published in the Annals of Internal Medicine later that year, and most recently in a commentary in this journal, failed to include the most basic and most significant data derived in a clinical trial. Missing from these reports of the DASH-Sodium Trial, which had a 2 × 3 factorial design, are the data on the trial’s primary endpoint—the means and standard deviations of the systolic blood pressure (BP) for each of the appropriate subgroups on the DASH and control diets at each of the three sodium intake levels assessed.

Although the investigators have widely promulgated the necessity of all Americans to reduce their dietary sodium intake to <2400 mg/day, they have not provided the data to justify this. In both published papers there are clear indications that the authors’ repeated claims are not supported by the limited evidence that they have provided pertaining specifically to the global interpretation that they place on the results. In Fig. 2 in the New England Journal of Medicine article and in Table 4 in the Annals article, it is evident that for individuals with normal BP, age <45 years, and not African American, once their overall diet quality was improved (DASH diet), restricting dietary sodium to <3300 mg/day had no further benefit.

The sweeping conclusions offered by the DASH-Sodium Trial investigators in their prior publications have been broadly and repeatedly amplified by Claude Lenfant, NHLBI Director, in press releases and cited prominently in recent policy publications of the NHLBI National High Blood Pressure Education Program. However, despite these widespread claims and national promotions, the data to support them remain undisclosed. The failure of the investigators to provide a full presenta-
tion of the data acquired in this trial prevents the medical community from determining once and for all whether the initial and repeated conclusions of the authors are valid.

Despite earlier and repeated requests\textsuperscript{12,13} that these investigators simply report the primary endpoint data, they have failed to do so. This is not a complex or unreasonable request; it can be simply met with a straightforward table reporting each subgroup’s actual BP response to the three sodium levels on the two diets. For the journal’s readers, imagine conducting a randomized controlled trial with a $2 \times 3$ factorial design and publishing two high-profile articles based on the trial, but never including a summary table of the mean changes in the primary endpoint of the trial.

In their first publication\textsuperscript{4} the authors provided “relative” changes in the BP for several (although not all) of the subgroups, but they never displayed the actual BP, thus making any objective assessment impossible. Although Sacks et al had assured readers of the New England Journal of Medicine that their second article would include subgroup analyses\textsuperscript{14} that article, by Vollmer et al\textsuperscript{5} exercised remarkable scientific and statistical license by dropping one entire limb of the trial (2400-mg sodium intervention). Despite the assurance of Sacks et al, that maneuver again circumvented the request to provide complete data, and again prohibited independent analysis that would have determined whether “all Americans” would indeed benefit from dietary sodium restriction once they were on the DASH diet.

In their recent AJH editorial\textsuperscript{6} the DASH-Sodium investigators and NHLBI once again failed to provide this most basic of data. Instead, they reiterated the use of “change in blood pressure”\textsuperscript{14} rather than providing the actual mean and SD blood pressure values, a statistical maneuver intended to obfuscate data interpretation. In the AJH article they also reproduced their subgroup analysis\textsuperscript{5} based on a model that eliminated one entire limb of the trial’s study design.

The persistent disregard by the NHLBI of the basic standards of reporting scientific data from the publicly funded DASH-Sodium Trial is a clear example of the need for the Data Quality Act. Skirting the best traditions of peer review and medical publication, the DASH-Sodium Trial investigators, with the obvious support of NHLBI, have failed to meet the reasonable standard of data disclosure. Coauthor William Vollmer’s recent comments in an interview in Science,\textsuperscript{3} which presumably refer to their recent AJH editorial,\textsuperscript{5} indicate his recognition that he and his colleagues have not complied with the requests for full disclosure. Vollmer states that there will be a paper that “may answer some of McCarron’s questions” [italics added]. Why may answer, and why only some of the questions? Why not provide the data and allow independent experts to answer all of the questions?

Why the resistance to meet such a simple and fundamental request? In the Science article, coauthor Lawrence Appel stated that data are being withheld because DASH-Sodium Trial investigators fear that those requesting them will “dredge the data.” One wonders whether the Chair of Biostatistics at Johns Hopkins University (Dr. Appel’s institution) would concur that performing such fundamental statistics on the mean BP of subgroups, which the authors themselves predesignated, in a $2 \times 3$ factorial design study is data dredging. It is unlikely. It is even less likely that such an expert would concur with Dr. Appel’s characterization of basic statistical analysis as being “of questionable scientific value.” In the same Science article, Vollmer tried another approach to justifying their behavior, stating that it was “reasonable to give researchers . . . three years to publish their results.” All of us would no doubt agree. However, once investigators allow any portion of their data to be used by the funding agency—NHLBI in this case—to create, influence, or otherwise modify current policy, their claim to a 3-year period is abrogated not only by the Data Quality Act but also by the definition of scientific integrity.

If NHLBI wanted the DASH-Sodium Trial data fully in the public domain, it would be there by now. It is plausible to assume that the reluctance of NHLBI may be based in its own conflict of interest in this matter. Dr. Lenfant and his colleagues at NHLBI have spent the better part of the past two decades championing sodium restriction\textsuperscript{15,16} as the most important dietary adjustment for the prevention and treatment of hypertension. Without the data to justify this, we must ask whether the vested interests of the NHLBI might not have a role in apparent efforts to protect this policy. Actually, once all of the necessary data are disclosed, they may well demonstrate that we have found, at last, an effective way to deal with the adverse effects of salt in some persons, i.e., through the DASH diet. Such an outcome would leave sodium restriction as an adjunct dietary option for a subgroup of hypertensive individuals—not the first and foremost approach for “all Americans” as Drs Lenfant, Sacks, Appel, and others espouse.

It is unfortunate that legal remedies have become necessary to ensure that data from publicly funded research is properly placed in the public domain. In fact, NHLBI elected to flaunt federal laws by failing to comply with the 60-day response period required by the Data Quality Act. NHLBI’s actions again strain its professional credibility, as there is no plausible reason not to have been able to provide the simple data as requested legally by the petition. However, a more realistic assessment might be that it has been naive to assume in the past that federal agencies can be both the source of funding and the interpreter of the results. In the end, agencies such as NHLBI are directed by humans who may be no different in their biases toward proving a hypothesis and sustaining its social impact than a senior scientist guiding a research project for a pharmaceutical company.

This is particularly true where hundreds of millions of dollars in research funds have been spent in the process. There is one big difference, however. The scientists working for and with an agency such as NHLBI are using

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public funds, and not the private capital used in the private sector. Just as we have strong checks and balances in place to ensure that data quality derived from private ventures is accurately and fairly interpreted, the Data Quality Act has been passed to ensure that the same standards hold sway in the public domain.

After three incomplete publications,\textsuperscript{4–6} it is clear that the peer review process will not succeed in assuring a full and transparent presentation of the DASH-Sodium data. I am confident that the facts will ultimately prevail through the process put in place with this act. One can envision other scientists closely monitoring the outcome of this first petition to NHLBI as they ponder whether it may be a means to clarify another contentious issue that our discipline faces, ie, NHLBI’s interpretation of the ALLHAT study.\textsuperscript{17–19} As the Data Quality Act becomes a reality and federal agencies realize that transparency in data presentation and interpretation can be no less of a commitment for them than it is in the private sector, we will likely see benefits to all members of society. This would be an appropriate outcome, bearing in mind that it is the American taxpayers who underwrite our federal research budget, and to whom we owe our best efforts to ensure a full and fair interpretation of the data.

References