Quality of data evaluation system (QODES) in clinical research publications

Fraud in clinical research is a problem that, to-date, has attracted little attention despite its potentially momentous implications. Clearly, fraud reaches its maximum expression when the results of a fraudulent study are presented to the scientific community, whether in the form of an oral communication (and published in the proceedings of the congress), or as an article in a medical journal. A good definition of fraud is that of the UK Medical Research Council which states: "Research misconduct or fraud means fabrication, falsification, plagiarism, or deception in proposing, carrying out or reporting results of research and deliberate, dangerous, or negligent deviations from accepted practices in carrying out research"¹. Within this definition of fraud are various manipulations of data that can be considered from more-or-less dubious up to that which are scandalous. Some of these manipulations, of which there are frequent examples in the recent history of clinical investigation, include the following: fabrication (invention) of data, falsification (deliberate distortion) of data, suppression of relevant parts of the data, devious manipulations in data analysis, fabrication (invention) or falsification (deliberate distortion) of the methodology of the study and plagiarism of data.

It has been about two years since I accepted the invitation of the *Revista de Oncologia* to write an editorial on the problem of fraud in clinical investigation². At that time the deplorable case of the South African Werner Bezwoda achieved considerable notoriety. Dr. Bezwoda fabricated and falsified data from a randomised study of breast cancer that compared conventional chemotherapy with intensive chemotherapy with autologous haematopoietic support³. This investigator was able to present, without difficulty, his fraudulent data orally at the prestigious plenary session of the 35th Annual Meeting of the American Society of Clinical Oncology⁴. Following the discovery of the fraud, Dr. Bezwoda was dismissed from his academic post at the University of Witwatersrand in South Africa⁵.

These major falsifications of data, despite the scandalous repercussion on the scientific community and the public media, are probably not the only, nor the

most frequent, fraudulent manipulations of results of clinical trials. Many of us have read a not-inconsiderable number of articles (usually single-institution studies not submitted to external data monitoring) published in prestigious journals which may be considered to have applied more subtle, but no less relevant, manipulation of data.

One subtle form of manipulation of data denounced recently by medical journals is the deliberate obscuring of parts of the results in studies promoted by the pharmaceutical industry; results which, if publicised, would adversely affect the financial interests of the promoting agency. In September 2001, 12 medical journals carried identical editorials, raising the alarm over the suspect objectivity of some published articles in which the pharmaceutical industry was the sponsor⁶. The editorials raised a storm of protests from the media close to the pharmaceutical industry. The gist of the complaints was the *a priori* assumption of integrity on the part of the investigator belonging to an academic institution while openly questioning the integrity of the pharmaceutical industry^{7,8}. Probably, both parties in the argument have some truth, but we would go much further by suggesting that medical journals also have a considerable responsibility since it is their vehicle that disseminates the fraud. Some editors of medical journals argue that interventionist practices, such as auditing the data of studies that are submitted for publication, are not within the remit of an editor and propose, instead, the creation of some type of Official Agency for this purpose. In the manner of a tribunal, the experts of this agency would convene in the case of suspected fraud⁹. Indeed, this type of agency has already been created in the United States, Denmark, Norway, Finland, Australia and other countries and can be called-upon any time a study is suspected of being fraudulently produced. However, an agency of this type cannot resolve the two principal problems: the detection and the prevention of fraud.

With current editorial practices, the process of "peer-review" of an article only serves to evaluate whether the results that the authors present are well described, that the statistical management that the authors

say have been performed are the appropriate ones and whether the conclusions of the study are supported by the data that the authors say they have obtained. The Reviewer does not have any way of ascertaining that the study was performed in accordance with the methodology that was described, nor that the data described correspond exactly to those actually generated in the study. As such, the process of peer-review is not efficient in detecting fraud. How then can we screen-out fraud in clinical investigation? I believe that the most fruitful way of prevention and of identification of fraud in communications at meetings and in journal publications would be to require the authors of a manuscript (or communication) to supply documentation that provides evidence of the various steps performed in the trial. Currently, clinical trials are regulated by legislation that is quite strict and which generates a profusion of documentation (structured protocol of the study, approval by the ethical committee of the institution, informed consent from the patient, data collection sheets, compiled database, statistical evaluations, final report of the study). Soliciting this documentation exerts a dissuasive effect on those investigators whose studies contain fraudulent information i.e. the author would not dare to provide this information for fear of having the fraud uncovered. At the same time, minor discrepancies could be identified which would preclude biased results being published. Finally, if there were some means by which the quality of data of an article can be quantified, we would have a yardstick of the quality of a study. This would be extremely useful for the readers of the article in gauging the reliability of the study.

Recently, the Federation of the Spanish Societies of Oncology (*FESEO, Federación de Sociedades Españolas de Oncología*) and the Mexican National Institute of Cancer (*Instituto Nacional de Cancerología de México*) honoured me by naming me Editor-in-Chief of their journal. My first contribution to *Revista de Oncología* will be to implement a system of quality control of data in publications of clinical trials. In accordance with this system, authors of articles related to clinical trials can voluntarily submit their manuscripts to an evaluation of data quality (quality of data evaluation system; QODES) and the application of which would assign a score to the manuscript. Manuscript submitted to this evaluation would need to include, within the Materials and Methods section, a statement referring to aspects of quality control of the data. This section is to contain a description of the steps taken to guaranty the veracity of the data. These would include information on patient registration, procedures for the randomisation of patients, methods of data collection, quality control measures (including external auditing) and the identification of the individuals responsible for the data handling as well as the statistical

TABLE 1. **Quality of data evaluation system (QODES)**

Items and score	
A. Final (definitive) protocol used in the study together with its date of approval	
0 points: protocol not supplied	
1 point: protocol supplied; but not coinciding exactly with that stated in the article	
2 points: protocol coinciding with the statements in the article, but not having the standard sections properly established or clearly defined	
3 points: protocol supplied; and coinciding exactly with the text of the article as well as structured in accordance with current standards	
B. Copy of the Ethical Committee Approval	
0 points: not supplied	
3 points: supplied	
C. Letter from the person or persons who performed the statistical analyses and who takes responsibility for correct handling of data and the veracity of the analyses. This person (or persons) must accept responsibility for responding to questions that may be put by the Editorial Committee (or the Reviewers designated by the Committee) in relation to these analyses	
0 points: not supplied	
3 points: supplied	
D. Copy of the registration file and, if applicable, the randomization file of the patients*, including data of registration/randomization	
0 points: not supplied	
1 point: supplied; prospective registration and randomization (if applicable) in the same institution where the study was conducted	
3 points: supplied; prospective registration and randomization (if applicable) in a centre of data management which is external to the centre in which the study was conducted	
E. Copy of the Case Report Form that was used in the study for data collection* (electronic version and/or hardcopy)	
0 points: not supplied	
1 point: supplied; but with important deviations from the protocol requirements	
2 points: supplied; but with slight deviations from the protocol requirements	
3 points: supplied; and coincides exactly with the protocol requirements	
F. Methodology and conduct of the study	
0 points: not coincident with that stated in the Materials and Methods section	
1 point: important deviations from that stated in the Materials and Methods section	
2 points: slight deviations from that stated in the Materials and Methods section	
3 points: coincident with that stated in the Materials and Methods section	
G. Monitoring (audit) of data	
0 points: study not monitored by persons dissociated from the investigators	
2 point: random or partial monitoring of data by persons dissociated from the investigators	
3 points: monitoring of all the relevant data by persons dissociated from the investigators	
H. Copy of the Database* used to generate the study results and in which are stored the data of each individual patient and reflecting all variables analysed in the manuscript	
0 points: not supplied	
1 point: supplied; but incomplete in some relevant aspects	
2 points: supplied; but incomplete in some less-relevant aspects	
3 points: supplied; and complete	

*The key that could identify the patients must be withheld so as to guaranty anonymity of the study subject.

analysis. If data recording and control are performed according to good clinical practice rules (i.e. Good Clinical Practice-International Conference of Harmonization Guidelines [GCP-ICH]), this should be specified as well. Further, the authors commit themselves to accepting an *in situ* audit of the data in the case the Editorial Board requires it and to provide information on the sponsor of the study together with the potential conflicts of interest. It will be up to the Editorial Board to decide if this information would need to be divulged in the published manuscript, or not. The authors should supply the necessary documentation to fulfil the QODES evaluation whose items and scoring are presented in table 1. The final score will be included at the end of the manuscript together with any clarifications that the Editorial Committee, as well as the Author, considers pertinent.

To assess the practicalities of the system, we submitted an article published in this current issue of the *Revista de Oncología* to the QODES¹⁰ system of evaluation. We are confident that in the immediate future other authors of manuscripts submitted to our Journal will want to have their articles put through this system of quality control. The current QODES system constitutes only an initial approximation of the solution to the problem and is, indeed, subject to modification and improvement. We await suggestions from our readers as well as the Editors of other medical journals. These could include new items for evaluation and improvements on the current scoring system so that, hopefully, the scale can be refined and be made more clear-cut when evaluating of the quality of data from clinical trials.

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