Review Article

Tiny tweaks, big changes: An alternative strategy to empower ethical culture of human research in anesthesia (A Taiwan Acta Anesthesiologica Taiwanica—Ethics Review Task Force Report)

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ABSTRACT

For this guidance article, the Ethics Review Task Force (ERTF) of the Journal reviewed and discussed the ethics issues related to publication of human research in the field of anesthesia. ERTF first introduced international ethics principles and minimal requirements of reporting of ethics practices, followed by discussing the universal problems of publication ethics. ERTF then compared the accountability and methodology of several medical journals in assuring authors' ethics compliance. Using the Taiwan Institutional Review Board system as an example, ERTF expressed the importance of institutional review board registration and accreditation to assure human participant protection. ERTF presented four major human research misconducts in the field of anesthesia in recent years. ERTF finally proposed a flow-chart to guide journal peer reviewers and editors in ethics review during the editorial process in publishing. Examples of template languages applied in the Ethics statement section in the manuscript are expected to strengthen the ethics compliance of the authors and to set an ethical culture for all the stakeholders involved in human research.

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1. The origin of the Acta Anesthesiologica Taiwanica—Ethics Review Task Force

On December 23, 2014, the Editor-in-Chief-Elect (Dr W.Z. Sun) of Acta Anesthesiologica Taiwanica (AAT) chaired a meeting in Taipei, Taiwan. During this meeting, Dr Sun proposed to develop a tool for the Editorial Office of AAT in order to solve any publication ethics issues, if there are any, in the past and in the future. Dr H.N. Luk was assigned to lead the team and charged to explore publication ethics issues of AAT. Dr Luk immediately proposed to establish the Ethics Review Task Force (ERTF) on December 24, 2014. The mission of the AAT-ERTF was proposed as follows: (1) to identify the publication ethics issues of the AAT in the past; (2) to assess the potential impacts of such ethics issues on the AAT; (3) to find a practical solution to empower publication ethics; and (4) to evaluate the outcome of such solution for ethics issues periodically. This proposal was included and documented in the meeting minutes of the meeting of December 23, 2014. At the same time, Dr Luk was assigned to prepare a series of publication ethics guidance papers for AAT Editorial Office and to submit one in the earliest issue of AAT in 2015.

2. International ethics principles

The Declaration of Helsinki (DoH) was most recently revised in October 2013.1 As a statement of ethical principles for medical research involving (living) human participants, including research on identifiable human material and data, the DoH is adopted worldwide. While the purpose of medical research is to generate new knowledge, it is subject to ethical standards that promote and ensure respect for all human research participants and protect their...
rights and welfare. It is the duty of physicians and scientists involved in medical research to protect the life, health, dignity, integrity, right to self-determination, privacy, and confidentiality of personal information of research participants.

The roles and functions of the Research Ethics Committee or Institutional Review Board (IRB) are stated in Article 23 of the DoH. One of the major requirements of a human research is that the research protocol has to be reviewed and approved by a qualified independent IRB prior to the beginning of the study. The standards of the policy and operation of IRB review and approval have to conform to both national laws and regulations and international ethics norms (e.g., the ethics standards in the DoH).

From Article 25 to Article 32, the DoH defines the requirements of informed consent from the study participants during human research. Although the DoH does not cover a wide range of increasingly complex ethical issues of informed consent, it does point out some important values and characteristics of the informed consent process. The DoH also touches on the issues of voluntariness, providing adequate and understandable information, documentation of consent, surrogate consent and assent, rights to refuse to participate and to withdraw from the study, vulnerable and dependent situations, identifiable human materials and data, etc.

Article 35 of the DoH states that every research study involving human participants must be registered in a publicly accessible database before recruitment (i.e., enrollment) of the first participant. The Article 36 of the DoH states that researchers, authors, sponsors, editors, and publishers have ethical obligations with regard to the publication and dissemination of the results of research. All parties should adhere to accepted guidelines for ethical reporting. Sources of funding, institutional affiliations, and conflicts of interest must be declared in the publication. Most important, reports of research not conducted in accordance with the principles of the DoH should not be accepted for publication.

3. The minimum requirements of clear reporting of ethics practices

Among all the stakeholders of human research, authors (investigators) and their affiliated institutions, study sponsors, journal editors (and peer reviewers), and publishers are all responsible for ethical conduct of human studies. According to the DoH, human research studies should be approved by an independent IRB and the investigators should seek informed consent from all study participants. These essential principles have in turn been addressed by the International Committee of Medical Journal Editors (ICMJE) and the Committee on Publication Ethics (COPE). Both groups have published core requirements for the conduct and reporting of human research findings. In order to review best practice and ethical standards in the conduct and reporting of research and other material published in medical journals, and to help authors, editors, and others involved in peer review and biomedical publishing create and distribute accurate, clear, reproducible, unbiased medical journal articles, ICMJE developed and revised the recommendations (previously known as uniform requirements for manuscripts) from 1978 to 2013.2,3 The ICMJE recommendations are adopted by numerous medical journals. The responsible and accountable authors should (or are expected to) use the ICMJE recommendations along with individual journals’ instructions for authors.

Regarding the reporting of ethics review of human study, ICMJE recommends the statement in the Methods section in submitted manuscript as follows: “The Methods section should include a statement indicating that the research was approved (or determined to be exempt from the need for review) by a responsible review committee (institutional or national). If no formal ethics committee is available, a statement indicating that the research was conducted according to the principles of the Declaration of Helsinki should be included. If questions exist as to whether or not the research was conducted in accordance with the DoH, the authors must explain the rationale for their approach and demonstrate that the institutional review body explicitly approved the ethically questionable aspects of the study.”2,3

In addition to the requirement of IRB review and approval, ICMJE also recommends a statement regarding study participants’ informed consent as follows: “Patients have a right to privacy that should not be violated without informed consent. Identifying information should not be published unless the information is essential for scientific purposes and the patient (or parent or guardian) gives written informed consent for publication. Informed consent for this purpose requires that an identifiable patient be shown the manuscript to be published. Patient consent should be written and archived with the journal, the authors, or both, as dictated by local regulations or laws. Applicable laws vary from locale to locale, and journals should establish their own policies with legal guidance. The author should provide the journal with a written statement that attests that they have received and archived written patient consent. Informed consent should be obtained if there is any doubt that anonymity can be maintained. The requirement for informed consent should be included in the journal’s instructions for authors. When informed consent has been obtained, it should be indicated in the published article.”2,3

The COPE code of conduct asks editors to ensure that reports of clinical trials cite compliance with the DoH, Good Clinical Practice, and other relevant guidelines on safeguarding study participants. It states: “Editors should ensure that research material they publish conforms to internationally accepted ethical guidelines (e.g., DoH).” Editors should seek assurances that all research has been approved by an appropriate body (e.g., IRB). However, editors should recognize that such approval does not guarantee that the research is ethical. Editors should protect the confidentiality of individual information (e.g., that obtained through the doctor–patient relationship). It is therefore almost always necessary to obtain written informed consent from patients described in case reports and for photographs of patients. It may be possible to publish without explicit consent if the report is important to public health (or is in some other way important); consent would be unusually burdensome to obtain; and a reasonable individual would be unlikely to object to publication (all 3 conditions must be met).”

4. The universal problems of publication ethics

Together, DoH, ICMJE, and COPE provide practical ethics standards and guidance for the authors (medical researchers), peer reviewers, and editors of the medical journals. During the manuscript review process and subsequent publishing, all these stakeholders of human research should particularly adhere to the ethics requirements in three major aspects: (1) to ensure that the submitted or published human research has been reviewed and approved by an IRB; (2) to ensure that effective informed consent has been obtained from the research participants; and (3) not to publish any unethical human research results.

In addition to the defined research misconduct (plagiarism, data fabrication, falsification, duplication, and redundant publication) that can undermine the science, other forms of publication ethics issues (e.g., noncompliance with ethics standards and norms) also play an important role in losing public trust. Surveys from journal editors show that some editors of medical journals seem not very concerned about publication ethics and believe that such misconduct occurs only rarely in their journals. Meanwhile, many editors
admitted that they are unfamiliar with available guidelines and would welcome more guidance or training.25,26

Public interest in issues concerning the maintenance of high ethical standards in the conduct of scientific and human research and its publication has increased in recent decades. Some of the developments in these issues as reflected in the publication of the specific requirements for authors for manuscript preparation as stated in the Instructions to Authors for articles being prepared for submission medical literature. The instructions to authors (or information for authors) of these journals contain the references to ethical standards or requirements (e.g., DoH, ICMJE). The ethical issues that the instructions most often cover are specifically related to the individual journal's publication requirements. The study results suggest that while the editors and publishers of the biomedical literature are concerned with promoting and protecting the rights of the participants in experiments in the articles they publish, and while these concerns are not yet paramount, they are evolving and growing in recent decades.33 As a result of the ever-increasing scrutiny from the public, news media, and government agencies, journals are recognizing the need for greater transparency in the peer review process and are thus more inclined to enforce ethical standards. The journals usually need to set policies and procedures comparable to those of the key publications on ethical issues (e.g., authorship criteria, conflicts of interest, redundant publication, data access and biases in data reporting, image manipulation) that authors should think it over before submitting a manuscript.34

The DoH recommends that publishers do not publish articles that fail to respect these procedures. The ICMJE requires authors of journal articles to state in their publications whether the study was done according to national or institutional ethical standards. Unfortunately, failure to report these ethical procedures in scientific publications has occurred in the past and continues to occur now. Instructions to authors regarding ethical standards have improved somewhat. Some remain incomplete, for example, regarding the scope of disclosure of funding sources and conflict of interests. The ethical guidelines presented to authors need further clarification and standardization.3–16

Basic ethics standards or requirement were not typically reported in publications in the past decades. The incidence of reporting IRB review and study participants' informed consent varied in many aspects, including different disciplines and specialties, geographical areas, types of clinical research, etc. For example, inadequate ethics compliance was reported when the clinical research involved vulnerable participants, such as elderly people living in the nursing home, newborns, children,27–29 aging patients,24,25 stroke patients,26 studies involving emergency medicine,21 and genetic studies.28

The phenomenon of inadequate ethics reporting exists in almost all ranges of scientific disciplines, e.g., in oral and maxillofacial surgery research,20,21 cardiovascular research,22 critical care medicine,21,23 emergency medicine,21,24 human immunodeficiency virus/AIDS research,25,26 psychiatry,27 complementary and alternative medicine,28 dental research,29–33 physical therapy,23–26 dermatology,27 otolaryngology,30 nursing,30,50 epidemiology.50 Phase 3 oncology clinical trials,26 and anesthesia.3,1–56

Inadequate ethics reporting in the biomedical research journals is a near universal phenomenon, but perhaps more problematic in some developing countries. For example, under-reporting has occurred in Cameroon,27 eastern Mediterranean regions,50,51 Spain,50 Portugal,24 Brazil,21,25,62 Egypt, Argentina,21,31 Chile, India, Iraq,30,57 Sri Lanka,18,62,63 Iran,63,64 and China.12 The high proportion of articles lacking ethical review in developing countries or regions suggests the presence of legal and ethical flaws that should be discussed and overcome in the near future.

During the past two decades, more and more medical journals require independent IRB approval of human research and most journals continue to require that this disclosure appears in the manuscript. Fewer medical journal instructions to authors provide no ethical guidelines for human research. For example, it is reported that 9% of studies still do not report IRB approval for human research.21 Consecutive series of research papers published in the Annals of Internal Medicine, British Medical Journal, Journal of American Medical Association, Lancet, and The New England Journal of Medicine between February 2003 and May 2003 were reviewed for the reporting of ethical approval and patient consent.24 Ethical approval and consent were not mentioned in 31% and 47% of manuscripts, respectively. In 27% of papers, the authors failed to report both approval and consent. The reporting of ethical approval and consent in randomized control trials has improved, but journals are less good at reporting this information for other study designs. It was concluded that journals should publish this information for all research on human participants. A few years later, a review of all 1133 clinical research articles published between 2005 and 2006 in four major clinical journals found that 3.2% lacked a statement of ethics approval and 5.5% lacked a statement of informed consent.50 Although medical journals increasingly require disclosure statements of relevant IRB approval for human research, most of them fail to verify such approval beyond taking authors for their word (i.e., no journal required submission of the study approval letter or of the approved protocol).73

Clinical researchers rarely described or discussed the rationale for ethically controversial features of study design or special procedures instituted to enhance the protection of participants taking part in research, or how to ensure an effective informed consent be obtained. An extensive reporting of pertinent ethical issues in the manuscript to promote public accountability for clinical research has been recommended.73 Recently, inadequate reporting of IRB's review and study participants' informed consent in cluster randomized trials has been concluded and discussed in a series of papers.74–77 For example, during the period from 2000 to 2008, out of 300 trials, 26% (n = 77) and 31% (n = 93) failed to report IRB review and report informed consent.74 Some explanations have been proposed, e.g., the nature of such cluster randomized trials and the different targeted study participants (at the cluster level or individual level).

In general, clinical trials that adhered to more rigorous methodological and reporting standards were more likely to report ethics approval and informed consent. Articles published in medical journals with higher impact factors (IF) were more likely to disclose ethics requirement, although the IF may be an imperfect surrogate for methodological and reporting quality indicator. We therefore can conclude that publication ethics issues have recently improved, but remain incomplete.

5. Journals' accountability

All the stakeholders in human research, including the journals and institutions, have to value ethical behavior (i.e., value the value). Journals have a moral role in providing an environment and ethical culture that emphasizes the importance of justifiable behavior in human research. Peer reviewers and journal editors are gatekeepers for the integrity of the scientific research and human study. They should try to enforce requirements for authors to meet ethical standards and, as stated in the DoH, reject (and retract) research not meeting these requirements (e.g., without IRB approval or participants informed consent).

Although many medical journals, including the examples mentioned in Table 1 of this article, now provide guidance on including information on ethics approval and informed consent in their instructions to authors, many do not enforce these
requirements effectively. Journal editors should consider some more effective mechanisms to ensure that adequate information is reported for all research involving human participants. Research granting bodies (e.g., governmental and institutional) and IRB also play a role in improving the standards of reporting by requiring including an ethics statement about IRB approval and participants’ informed consent in all publications from projects they approved and funded.

A few journal editors accept scientifically worthy papers that lack an ethical review process, but attach an editorial comment to the end of such papers when published. The comment points out the ethical flaw, explains how the flaw was weighed against the scientific value of the study, and expresses support for an ethical process in research involving human participants. Whether the society allows any unethical human research results to be published or even used remains an ethics controversy.

It is understandable that an editorial office of a medical journal, with limited human and financial resources, is not able to serve as moral police. The editorial office cannot assure that the authors (researchers) are morally right in the human study. However, the peer reviewers and journal editors of medical journals should take all the steps necessary to assure their readers that the contents of the publications are based in science done with integrity and that have met the ethical rules and standards of biomedical and clinical research, including the reporting. Due to the fact of publish or perish, increasing instances of misconduct in medical scientific publications are noticed. The role and responsibility of peer reviewers and journal editors have become increasingly difficult and heavy. Honesty and good faith in all the moral actors involved in the process of biomedical publications and human research (authors, peer reviewers, editors, IRB, institutions) remain the cornerstones of scientifically and ethically good conduct.

### 6. Current status of IRBs in Taiwan

In order to control the quality review of the IRB, there are two possible mechanisms to reach such a goal: internal audit and external evaluation. Internal audit can be done by the IRB office itself or the human research participants’ protection (HRPP) program in the hospital or institute. External evaluation can be done by either the national health regulatory authority or an independent international organization. In Taiwan, the Ministry of Health has started a domestic IRB registration and inspection program in 2005. Up to 2014, there are 83 IRBs to have received registration and inspection by Taiwan Joint Commission on Hospital Accreditation. The official accreditation of IRB by Taiwan Joint Commission on Hospital Accreditation has been a required element of hospital accreditation in Taiwan.

The Forum for Ethical Review Committees in the Asian and Western Pacific Region was established in 2000 under the project of Strategic Initiative for Developing Capacity in Ethical Review from the World Health Organization–Special Program for Research and Training in Tropical Diseases. There are five such fora in each continental region (Asia—Pacific, Africa, Latin America, North America, and Eastern Europe). Up to 2015, >200 IRBs in Asia have been recognized by Forum for Ethical Review Committees in the Asian and Western Pacific Region. Among them, there are 23 IRBs from Taiwan.

The Association for the Accreditation of HRPPs (AAHRPP) is an American research organization. As of 2014, 205 IRBs have been accredited by AAHRPP in USA. Few of them are from Taiwan, Korea, China, Singapore, Thailand, India, Saudi Arabia, etc. As of 2015, there are two IRBs in Taiwan that have obtained AAHRPP accreditation and two others are undergoing the accreditation process.

In order to control and improve the quality review of IRB, both national and international accreditation, survey, or evaluation programs have been set up and implemented in some countries and regions. Table 2 shows the similarities and differences among three systems. Even though there are some technical differences among the three survey systems, the goals and essential principles are similar. Although the IRB evaluation and accreditation mechanisms cannot guarantee any occurrence of unethical human research in those institutions, such audit and inspection can definitely add one more layer of assurance on IRB functions and performance. Namely, when receiving any submitted manuscripts involving human research that need IRB review and approval (and probably need study participants’ informed consent), the reviewers and editors of medical journals might feel more confident and comfortable on the credibility of those qualified IRBs that have been registered and accredited.

Although DoH and other international ethics guidelines require IRB review and approval of human research, the exact number and qualification of IRBs in the real world are still unknown. While the IRB registration system does not exist in many advanced countries

### Table 1: Comparison of ethics requirements among several medical journals.

<table>
<thead>
<tr>
<th>Requirement</th>
<th>NEJM</th>
<th>Lancet</th>
<th>Anesthesiology</th>
<th>AA</th>
<th>AAT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Required compliance with URMs of ICMJE</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Setting standards of ethical research conduct for the authors</td>
<td>++</td>
<td>++</td>
<td>++</td>
<td>+++</td>
<td>+</td>
</tr>
<tr>
<td>Explicitly required compliance with DoH and refused to publish any unethical study results</td>
<td>Nill</td>
<td>Nill</td>
<td>Nill</td>
<td>X</td>
<td>Nill</td>
</tr>
<tr>
<td>Required Ethics statement section in the manuscript</td>
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<td>Nill</td>
<td>Nill</td>
<td>Nill</td>
<td>Nill</td>
</tr>
<tr>
<td>Required submission of COA</td>
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<td>Nill</td>
<td>Nill</td>
<td>Nill</td>
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</tr>
<tr>
<td>Statement of IRB’s approval in the Methods section</td>
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<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
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<td>Nill</td>
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<td>Statement of COA serial number</td>
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<td>Nill</td>
<td>Nill</td>
<td>Nill</td>
<td>Nill</td>
</tr>
<tr>
<td>If without COA, required a statement of compliance with DoH</td>
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<td>Nill</td>
<td>Nill</td>
<td>Nil</td>
<td>X</td>
</tr>
<tr>
<td>Statement of obtaining IC in the Methods section</td>
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<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Identification and justification of major ethics issues in the Methods section</td>
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<td>Nill</td>
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<td>Statement of IRB registration status</td>
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<tr>
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<td>Require provision of IRB’s contact information</td>
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<td>Statement of requesting copies of COA and ICF from authors</td>
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<td>Nill</td>
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<td>Nill</td>
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<tr>
<td>Statement regarding the editorial office reserve the right to contact responsible entity in the institution for clarifying and verifying ethics issues</td>
<td>Nill</td>
<td>Nill</td>
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</tr>
<tr>
<td>Required compliance of CONSORT</td>
<td>Nil</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Required clinical trial registration code and written down in the Methods section</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
</tbody>
</table>

AA = Anesthesia and Analgesia; AAT = Acta Anesthesiologica Taiwanica; COA = certificate of approval; CONSORT = Consolidated Standards of Reporting Trials; DoH = Declaration of Helsinki (version 2013); IC = informed consent; ICF = informed consent form; ICMJE: International Committee of Medical Journal Editors; IRB = Institutional Review Board; NEJM = The New England Journal of Medicine; URMs = Uniform Requirements for Manuscripts Submitted to Biomedical Journals: Writing and Editing for Biomedical Publication.

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and regions, some are under construction. Without an official IRB registration system or assurance system, there is no way to control the qualification and review quality of IRBs. In addition, there will be no platform to provide fixed training curriculum for IRBs or clinical researchers.

It is believed that better reporting and better registration of clinical trials that include substantial information will definitely improve the understanding, credibility, and unbiased translation of clinical research findings. All the stakeholders in human research might benefit from improved author instructions and ethics requirement in medical journals. While requiring adherence to the broadly accepted reporting guidelines and to clinical trial registration are important, to identify the status of IRB (registration and accreditation) is also crucial to ensure the scientific and ethics integrity of human research.

7. Chance or necessity

Although the development of human research participant protection evolved decades ago worldwide, examples of scientific misconducts and events of unethical human research are not uncommon. Such occurrence of ethics scandals is irrespective of countries or regions. Noncompliance or violation of human research ethics occurred in both developed and developing countries. Several examples in anesthesia research are presented as follows.

7.1. Case 1

Scott Reuben, an American anesthesiologist and prolific clinical researcher, was an influential expert of pain management. Reuben published not only the original clinical trials reports, but also the review articles that serve as clinical guidelines for clinicians. Reuben initially fell under suspicion when a routine hospital audit in 2008 found that he had never obtained IRB approval for two clinical trials that he had intended to present in a scheduled meeting in the hospital. After a 1-year internal investigation, Reuben finally admitted to fabricating and inventing the data underlying his human research. It turns out that Reuben never conducted the clinical trials that he wrote about in 21 journal articles, which can be dated back to 1996.

The hospital requested the journals to retract Reuben’s publications, which reported favorable results from several painkillers manufactured by major pharmaceutical companies, e.g., Pfizer, Merck, and Wyeth. The impact on the clinical field was huge because many practitioners had been using the findings in Reuben’s publications as guidelines for appropriate treatment regimens. Reuben’s academic misconduct was reported by mainstream media as “what may be considered the longest-running and widest-ranging cases of academic fraud” and “Reuben is the medical equivalent of Bernie Madoff.” Ten out of Reuben’s 21 fraudulent articles were published in Anesthesia & Analgesia and Steven Shafer is the editor-in-chief of that journal. Shafer issued notices of retraction in 2009. Shafer then made a remark that “Reuben’s misconduct is the biggest case of fraud in the history of anesthesiology.” Shafer was wrong. Reuben did not hold the world record of fabricating human studies for long. Very quickly, Reuben would be surprised that he is never alone in the world of fabrication and falsification.

7.2. Case 2

Joachim Boldt, a highly prolific German anesthesiologist, was considered a leading researcher into colloid and intravenous fluid management. He published dozens of papers proving (showing) colloid’s benefits and contradicting studies that suggested that colloid could actually increase the risk of death in patients receiving surgery and cause kidney failure, severe blood loss and heart failure. It was later found that Boldt received funding (financial sponsorship) from manufacturers of hydroxyethyl starch (HES, the colloid he most strongly advocated), including big companies such as B. Braun, Baxter, and Fresenius Kabi. According to news media reported, Boldt was frequently paid to speak at international medical conferences where he hailed HES as the holy grail of fluid management medications. It should be mentioned that HES and other colloid products are several times more expensive than the alternative fluid management drugs, crystalloids, which some doctors believe are much safer as crystalloids contain smaller molecules and are more easily absorbed perioperatively.

In 2009, one of Boldt’s articles comparing albumin and HES priming cardiopulmonary bypass was successfully published in Anesthesia & Analgesia. In 2010, this paper was retracted by Steven Shafer for lack of IRB approval and patients’ informed consent. A subsequent official investigations conducted by the German health authority concluded that the study was actually fabricated. Based on the concluding evidence, German authorities later determined that some other studies were conducted without IRB approval at all and Boldt’s studies “failed to meet required standards, including false data and clear evidence of procedural irregularities and research misconduct.” In 2011, Steven Shafer finally announced that Anesthesia & Analgesia retracted 22 papers written by Dr. Boldt for unethical research conduct. In addition, >88 papers published elsewhere by Boldt were eventually retracted by 18 journals in March 2011.

In Germany, Boldt received criminal charges against his forgery of documents and signatures, conducting drugs trials on patients without their consent and no official approval, and fraudulently claiming payments for operations he had never performed.
Germany, failing to obtain the approval of the IRB is a criminal offence. Boldt was then called the great pretender and has become one of the notorious examples of unethical human research. However, it should be noted that in all his published articles, Boldt made such statements as “After approval from the Ethics Study Board of the hospital, informed consent was obtained from the patients’ families.” The journals usually accepted his assurance without any doubt. In 2014, the last article was eventually retracted by Anesthesia & Analgesia.

Since then, Anesthesia & Analgesia has made some changes to its guidance for authors (http://edmgr.ovid.com/aa/accounts/GuideforAuthors.pdf). Few such requirements are as follows. (1) All authors on a paper must now sign to say they have seen the original data. (2) Authors must also state the name of the ethics committee or institutional review board that approved the study. (3) All editors of journals before publishing a piece of research should hold a copy of the statement of approval of the ethics committee. (4) Clinical trial registration with a code number is stated.

### 7.3. Case 3

Yoshitaka Fujii, an unbelievably prolific Japanese anesthesiologist, published >249 papers between 1993 and 2011. Fujii’s main research interest was clinical trials of medications to treat post-operative nausea and vomiting. In 2000, however, one of the Fujii’s clinical reports was questioned, as “the results are incredibly nice!” Such challenge and doubt were not resolved until another challenge in 2012. Based on overwhelming statistical evidence of fabrication, a series of official investigations responding to allegations against Fujii started in April, 2012.

Among the 172 papers (out of 212 articles) judged bogus, the Japanese official investigational report claimed that 126 studies of randomized, double-blind, controlled trials conducted by Fujii “were totally fabricated”. Actually, Fujii started falsifying data in 1993 and found a pattern of fabrication and falsification. While still struggling for survival, Fujii responded as such: “I want to answer it seriously, but I am not a statistician. I can only offer a few elements of rebuttal at this point. The only thing I can say is that we performed the tests over years with full honesty and integrity. Additionally, I did not write these articles alone, and some of data were collected by others as well.”

In 2013, Steven Shafer again issued an editor’s note in the Anesthesia & Analgesia and eventually retracted Fujii’s 23 articles published in the journal, after confirming Fujii’s misconduct. The aftermath of Fujii’s scandal is at least 209 research papers of dubious credibility. Fujii has set the new world record for faking research articles!

### 7.4. Case 4

Wai-Meng Ho is a Taiwanese anesthesiologist. He conducted a series of human studies in patients receiving cardiac anesthesia and published three articles, including in Anesthesia & Analgesia. In his horrific clinical studies, Ho inserted a catheter into cardiac patients’ jugular bulb in order to withdraw blood from their brain. While these cardiac patients were receiving heart surgeries, such an invasive procedure (catheterization into jugular bulb) was not a standard routine procedure and the patients got no therapeutic benefits at all. For pharmacokinetics studies, however, Ho needed patients’ blood from the brain to analyze when the patients were awake before anesthesia induction and under anesthesia during operation (to study the effects of inhalational anesthetics). Therefore, all the poor and uninformed vulnerable patients had to receive the unnecessary invasive procedures and blood withdrawal while being awake (just imagine how much stress the patients suffered from this unethical intervention!). A series of blood sampling was performed before and after anesthesia. In all of his three publications, Ho made such ethics statement in the section of Methods as: “Written informed consent was obtained from all patients and the Institutional Review Board of the Veterans General Hospital, Tai-chung, Taiwan, approved the study.” Not so surprising!

In 2005, a nosy American whistleblower (C.Y. Lin, a research competitor and renowned cardiac anesthesiologist in the USA) alleged that Ho’s clinical studies were against scientific principles and theoreies (an argument on uptake of inhalational anesthetics). While receiving and reviewing Lin’s complaints against Ho, the IRB found out a more serious problem than scientific arguments Lin brought up with. Ho never obtained IRB’s approval or patients’ informed consent for conducting such human research for years. Namely, all the ethics statements Ho made in his articles were fabricated.

During internal investigation by the institution, Ho made different versions of arguments (or lies) regarding lack of IRB approval and patients’ informed consent. Ho’s response and defense statements are as follows. (1) At the beginning of the inquiry, Ho insisted that he indeed had obtained both approval and informed consent. (2) Ho refused to provide original copies of the IRB approval letters and patients’ informed consent forms to the investigation panel. (3) Ho refused to provide the study raw data, experimental records, or enrollment lists of study participants to the investigation panel. (Note: Ho claimed that all the computer records and printed materials were lost.) (4) Later, although lacking any IRB approval, Ho claimed that an IRB approval was not necessary because he had been granted the human research projects with funding by the hospital administration. (Note: In the conditional approval of Ho’s research proposal, Ho guaranteed that an IRB approval and informed consent should be obtained before he was allowed to initiate the human studies.) (5) Ho claimed that he had obtained patients’ “oral” consent, although not the written informed consent as described in his articles. (Note: No evidence shows that Ho obtained any “oral” consent.) (6) Later, Ho changed his story again by saying that “research” informed consent was not necessary because the patients had signed “therapeutic” informed consent (the routine consent for surgical operation and anesthesia). (7) Ho claimed that all the clinical studies he had conducted were not under the scope and definition of “human research”. Therefore, he insisted that such clinical studies were not required to have IRB approval or patients’ informed consent. (8) Ho claimed that participants’ informed consent was not necessary because he only “collected” blood samples from human bodies. (9) Finally, Ho lied, stating that human research protection was not required during that period (from 2000 to 2005) in Taiwan. Therefore, Ho claimed there was no need to have IRB approval and participants’ informed consent for his conducting human studies. (Note: In Taiwan, IRB review and approval has been required since 1996 when Good Clinical Practice was legally adopted. The IRB of the hospital was established in 1988 and enforced relevant human research regulations in 1997. Ho conducted his clinical studies from 2000.)

As a last resort, in January 2006, Ho’s co-author (K.C. Wong) in these three publications handed over a piece of paper to the IRB special investigation panel. On that tiny piece of paper, only a few sentences were printed out: “When they conducted these studies, the authors’ practices conformed to the prevailing ethical standards in their institution at that time. The need for informed consent for the type of study in question appears either not to have existed at all, or to have been widely ignored.” Wong requested the IRB to consider and accept his version of the story and wish the IRB to close the case peacefully and quickly. The IRB special panel immediately turned down Wong’s irrational, illegal, and unethical
request. (Note: K.C. Wong died a few months later, after he made his last request to the IRB.)

Ho's case did not end after K.C. Wong’s death. In April 2006, Ho brought his case to the court in Taiwan. Ho argued that the IRB and the hospital administration had no rights or jurisdiction oversight authority to suspend and terminate his human research projects even though he violated all the ethics principles. Ho insisted that he had “rights” to continue his human studies, even though he failed to have IRB approval and participants’ informed consent. On October 24, 2006, after 6 months back and forth, the court eventually reached the rightful conclusion. The court recognized that Ho had violated all the ethics principles and national regulations for human research. Therefore, the court overruled Ho's re-appeals. Ho was not allowed to continue all of his ongoing human studies projects. (To access the court's verdict, see the final report, pages 73–89: http://wwwexam.gov.tw/public/Data/01131233871.pdf)

In spite of due diligence of the IRB and the court in Taiwan, Ho's case did not end rightfully and correctly. In December 2006, 2 months after the court's verdict on Ho’s case, the Editors-in-Chief of the three journals (including Anesthesia & Analgesia) made a peculiar move. They orchestrated an editorial article to discuss the Ho case.34 In this Editorial, David Bogod (the editor-in-chief) made a self-contradictory and ambiguous story. The context of this Editorial appears to obscure the facts and with double-talk. Bogod (and Steven Shafer must agree with) finally had to admit that Ho unambiguously fabricated all the ethics statements about IRB approval and participants' informed consent in the three publications.92–94

However, trying to make an excuse not to retract all those unethical articles by the journals (the rule as DoH and ICMJE mandated), Bogod needs to reconcile the “smoking gun” facts. Bogod eventually found his pretext in the Editorial: “When they conducted these studies, the authors' practices conformed to the prevailing ethical standards in their institution at that time. The need for informed consent for the type of study in question appears either not to have existed at all, or to have been widely ignored.” Sounds familiar?

The simple question is: Why did Bogod and Shafer insist on not retracting unethical human research publications? Bogod wrote his Editorial with the title of The editor as umpire and saw Ho’s misconduct case as a “dispute” between a whistle blower and the unethical authors. However, is fabrication of IRB approval and participants’ informed consent ever a “dispute”? Is noncompliance or violation of ethics principles and human research regulations ever a “dispute”? Is cheating or dishonesty ever a “dispute”? Is harming patients for research purpose ever a “dispute”? Whether it is a “dispute” in Ho’s case can only be answered by persons with integrity and sound moral value. Apparently, Bogod and Shafer could not answer that simple question.

It is not clear at all why the three renowned Editors-in-Chief of the anesthesia journals (Anesthesia, Anesthesia & Analgesia, and Acta Anaesthesiologica Scandinavica) took the words of Ho and his co-author but ignored the official investigational reports from the IRB and the verdict from the Taiwan court. Interesting to know, in all of these three articles,92–94 Ho’s major co-author was K.C. Wong who served on numerous editorial boards of anesthesia journals and the president of IARS (a famous academic society of anesthesia in USA). It is fair to say that friendship and collegiality are important, but character and integrity definitely should be more so. If Steven Shafer would have correctly and rightfully withdrawn Ho's unethical research papers in 2006 and thus set a good ethics example for all researchers in the field of anesthesia, Shafer might not have needed to be busy writing the notices of retraction years later for the Reuben’s case (in 2009); Boldt’s case (in 2010); and Fuji’s case (in 2013).

All the above-mentioned scandalous cases in anesthesia share one common feature: all the authors stated in their published articles that they had “IRB approval and participants’ informed consent”, as the journals guidelines required. Such requirement of statement in the articles apparently cannot prevent noncompliance and violation of ethics for the researchers. Actually, it has become a ritual and formality for publication. It does not matter whether the countries have already had well-established ethics oversight systems with proficient IRB review capacity (e.g., USA, Germany) or those are on their way to improve (e.g., Japan, Taiwan): ethics misconducts do occur everywhere. Therefore, the simple assurance of ethics conduct of human research with a vague statement in the manuscript is weak and vulnerable. An empowering mechanism is needed.

8. Tiny changes, significant assurance

On the basis of the DoH, most journals made their own integrity requirements for publication. For example, Anesthesia & Analgesia requires that all manuscripts reporting clinical research state in the first paragraph of the Methods section that: (1) “The study was approved by the appropriate Institutional Review Board.”; and (2) “Written informed consent was obtained from all subjects, a legal surrogate, the parents or legal guardians for minor subjects, or that the requirement for written informed consent was waived by the Institutional Review Board.”

As mentioned earlier, such simple and vague statements in the manuscript required by the journals did not effectively prevent or stop those researchers from fabricating or falsifying the ethics approvals and study participants’ informed consent. It appears that an extra layer of assurance mechanism should be considered and implemented.

9. Some key questions should be asked

Before we propose some changes to deal with publication ethics issues, we first ask whether currently the reviewers and editors have been provided with any practical ethics guidance to follow during the review process. In addition to conduct scientific review, the peer reviewers and editors of medical journals need to go through some kind of checklists that contain certain ethics issues of the human research. AAT-ERIF proposed the following 12 points to consider as guidance for peer reviewers and editors of the Journal.

(1) Is there a statement of compliance of ethics principles included in the manuscript?

Consistent with the mandate of the World Medical Association, DoH is addressed primarily to physicians. The World Medical Association encourages others who are involved in medical research involving human participants to adopt these principles (Article 2). Other ethics principles, such as the Belmont Report, could also be used as ethics guidelines for human research investigators worldwide. DoH also requires that the research protocol should contain a statement of the ethical considerations involved and should indicate how the principles in the DoH have been addressed (Article 22). Similarly, ICMJE recommends that the Methods section of manuscripts should include a statement indicating that the research was approved or exempted from the need for review by the responsible review committee (institutional or national). If no formal ethics committee is available, a statement indicating that the research was conducted according to the principles of the DoH should be included (ICMJE). Although it is usually assumed that all the researchers acknowledge, follow, and comply with ethics principles and national human research regulations, a statement of compliance of ethics principles in the manuscript do provide an extra layer of assurance for all the stakeholders in human research.
After all, reports of research not in accordance with the principles of the DoH should not be accepted for publication (Article 36). Peer reviewers and journal editors should not ignore the importance of requiring authors to make explicit statement of compliance of ethics principles in the manuscripts. The following statement is an example. “The authors assured and certified that this research has been conducted in accordance with all the ethics standards required by the Declaration of Helsinki issued in 2013.”

(2) Are the purpose and design of this human study ethically justified?

DoH requires that medical research involving human participants must conform to generally accepted scientific principles (Article 21). However, in additional to evaluating the scientific validity and integrity of a human study, the peer reviewers and journal editors need to check the ethical acceptability of the human research. DoH requires that human research is subject to ethical standards that promote and ensure respect for all human participants and protect their health and rights (Article 7). DoH also states that, while the primary purpose of medical research is to generate new knowledge, this goal can never take precedence over the rights and interests of individual research participants (Article 8). The individual research participant’s right to self-determination, privacy, and confidentiality of personal information are required to be protected (Article 9). When medical research is combined with medical care, the value of the study should be justified. Most important, the patient’s health, welfare, and rights should not be adversely affected (Article 14). The aforementioned four statements in DoH can be used as a general rule. In practice, the peer reviewers and editors should pay attention to the following issues. (1) What were the potential risks involved to the research participants in this study? (2) If there were any risks to the research participants, how were those risks minimized in this study? (3) What were the anticipated benefits to the individual participants (or to group of people, community, society, or to generate certain important knowledge) in this study? (4) Was the risks/benefits ratio reasonable to the individual participants in this study? (5) Was selection of participants equitable in this study? (6) Were vulnerable participants, disadvantaged participants, or sensitive research involved in this study?

(3) Is this human research exempted from IRB review?

DoH requires that the research protocol must be submitted for consideration, comment, guidance, and approval to the concerned research ethics committee (research ethics committee or IRB) before the study begins (Article 23). Unless meeting the criteria for exemption from IRB review and approval, all the human studies need to be approved by a formally organized IRB. Such criteria for exemption from IRB review and approval vary among countries and regions. Each country or region may have its own laws and regulations to govern human research, including the composition of IRB and criteria for exemption from IRB review. DoH stresses that physicians must consider the ethical, legal, and regulatory norms and standards for research involving human participants in their own countries as well as applicable international norms and standards. No national or international ethical, legal, or regulatory requirement should reduce or eliminate any of the protections for research participants set forth in the DoH (Article 10). That means, even from countries without relevant human research regulations, that the authors of the manuscripts have to give reasons why such human studies warranted an exemption from IRB review. The editors should justify such reasons and also require those reasons be clearly stated in the manuscripts for publication. The following criteria for the exemptions from IRB review have been applied by regulatory authorities in many countries. The peer reviewers and journal editors can use the following criteria as guidance while reviewing the manuscripts. (1) Research conducted in established or commonly accepted educational settings, involving normal educational practices. (2) Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures, or observation of public behavior (under 2 specific conditions). (3) Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures, or observation of public behavior not exempt under the previous paragraph, if: the participants are elected or appointed public officials or candidates for public office; or statute(s) require(s) without exception that the confidentiality of the personally identifiable information will be maintained throughout the research. (4) Research involving the collection or study of existing data, documents, records, pathological specimens, or diagnostic specimens (under 2 specific conditions). (5) Research and demonstration projects which are conducted by or subject to the approval of department or agency heads, and which are designed to study, evaluate, or otherwise examine public benefit or service programs, etc. (6) Taste and food quality evaluation and consumer acceptance studies (under 2 specific conditions).

It should be noted that, even if human participant research is exempt from the requirement for IRB review, the ethical principles (e.g., need for informed consent) apply.

(4) Is this high-risk human research?

DoH states that, in medical practice and in medical research, most interventions involve risks and burdens (Article 16). All medical research involving human participants must be preceded by careful assessment of predictable risks and burdens to the individuals and groups involved in the research. Measures to minimize the risks must be implemented. The risks must be continuously monitored, assessed, and documented by the researcher (Article 17). DoH re-emphasizes that the risks need to be adequately assessed and satisfactorily managed before the researchers may be involved in such research study (Article 18). In order to enhance human participant protection via improving effective ethics review process, the limited manpower and resources (for independent review) should be focused on those human studies posing greater than minimal risks. If the submitted manuscripts involved human studies exposing study participants to high-risks, peer reviewers and journal editors should be alert and determine whether all the risks have been identified and managed in the studies. More assuring indicators should be required, e.g., ensuring adequate IRB review and approval, sufficient, and effective informed consent, etc. The following points regarding the study risks need to be routinely considered by peer reviewers and journal editors. (1) Level of risks to the study participants: no more than minimal risks versus high risks. (2) Nature of risks: physical, psychological, social, etc. (3) Uncertain risks versus reasonably foreseeable risks (4) Issues of privacy, confidentiality, and stigmatization. (5) Characteristics of the study participants. (6) Local research context, local and national norms. (7) Unique cultural, educational, and religious factors. (8) Measure to reduce or minimize the risks.

(5) Does this study have an acceptable risk/benefit ratio?

DoH demands that medical research involving human participants may only be conducted if the importance of the objective outweighs the risks and burdens to the research participants...
(Article 16). Such human research must be preceded by careful assessment of foreseeable risks and burdens in comparison with reasonable benefits (Article 17). When the risks are found to outweigh the potential benefits, physicians must assess whether to continue, modify, or immediately stop the study (Article 18). All the stakeholders of human research are required to ensure that risks/benefits relation of such human study be reasonable and ethically acceptable. Several theories have been proposed for such tasks as follows: (1) component risk analysis; (2) net risk test; (3) direct comparative risk analysis; and (4) decision theory.

The peer reviewers and journal editors should check, from various information sources, and agree with such a conclusion (a reasonable risks/benefits ratio).

(6–8) Credibility of IRB review and approval

DoH requires that the research protocol must be submitted for consideration, comment, guidance, and approval to the concerned IRB before the study begins. This IRB must be transparent, independent, and duly qualified (Article 23). As mentioned earlier, most journals only require authors to state, “The study was approved by the appropriate Institutional Review Board.” in their submitted manuscript. While most careless investigators treated such a copy-and-paste statement as a formality, something more than such sentence can provide an extra layer of assurance to all the stakeholders of human research. Therefore, if the journal requires authors to add up the following information in the manuscripts and later the published articles, the general public (and all the stakeholders) can easily identify the credibility of the review quality of human participant protection from the publication: (1) IRB’s name; (2) the status of IRB for national (or international) registration; and (3) the status of IRB accreditation nationally or internationally.

(9) Is the claimed IRB approval provided with a serial number of the certificate of approval?

Although there is no requirement to publish the serial number of approval letter (certificate of approval; COA) of IRB, some journals do require the authors to provide the copied file of the COA to the editorial office. If the authors have to cite the serial number of the COA in the manuscript, this extra requirement can cause a second thought for the authors if they really plan to fabricate the IRB approval in the manuscript. Someone may argue that such a requirement increases the burden, inconvenience, or cost for publication. In current practice, however, most journals allow the authors to cite the grant numbers for sources of research funding in the Acknowledgments section. Apparently, citation of serial numbers does not cause any inconvenience or burden at all.

(10) Is this clinical trial identified in the clinical trial registration database?

DoH requires that every research study involving human participants must be registered in a publicly accessible database before recruitment (enrollment) of the first participant (Article 35). All parties should adhere to accepted guidelines for ethical reporting (Article 36). ICMJE also requires, as a condition of consideration for publication, registration in a public trials registry. As such, the registration datasets at least serve one of the sources to ensure the validity of human studies and trials. Therefore, the peer reviewers and journal editors should check whether the unique identifier of the registered clinical trial is valid and cross check the information both in the manuscripts and registration data. The following websites are examples of such clinical trial registration: https://clinicaltrials.gov/; https://www.clinicaltrialsregister.eu/ctr-search/

(11) Is written informed consent obtained from all the study participants?

The core value of human research is the respect for the study participants. Such respect is reflected by the requirement of an effective informed consent process prior to the human study. DoH requires that participation by individuals capable of giving informed consent as participants in medical research must be voluntary (Article 25). DoH also describes the essential and alternative elements of informed consent under general and special conditions (Articles 26–32). In addition, requirement of informed consent is applicable for the issues of post-trial access (Article 34) and unproven interventions in clinical practice (Article 37). Although most journals require a statement as “Informed consent was obtained from all participants,” in the Methods section of the manuscript, in practice, there is no mechanism to assure such informed consent process be effective and authentic. We hope that all the steps in the flow-chart (Fig. 1) may serve as an extra layer of assurance mechanism.

(12) Are there sources other than the authors available in order to verify the information when needed?

If the authors are at risks to fabricate and falsify the submitted information in the manuscript, the last resort to early detect and verify such misconduct is to make a direct contact to the relevant institutional representatives (GCP office, medical research department, IRB, HRPP office, etc.) or local governed authority (Ministry of Health and Welfare, Ministry of Education, etc.). Such a statement of possible contact should be included in the submission guidelines as information for authors.

10. Template languages in the text

The contents of the flow-chart (Fig. 1) represents the practical means for peer reviewers and journal editors to ensure ethics compliance by the authors. In order to substantiate such purpose to
empower the ethics culture of human research in the medical and academic community, a little bit more effort is required to proof against the failure to obtain ethics approval and informed consent by the researchers.

We here recommend adding a paragraph in the Ethics statement section. A few examples of template languages are as follows:

10.1. Example 1

This study is nonexempt human research and therefore was approved by XXX-IRB on 20YY-MM-DD (COA number: ZZZZZZ). XXX-IRB is a registered and accredited IRB. This research team has obtained the study participants’ effective informed consent prior to the outset of the research. The Journal has identified that this study posed high risks to the study participants, the Editorial Office reserves the rights to verify the validity of the COA and ICF via available alternative sources, when needed. Significant ethical issues related to this study have been identified as … It is reasonably believed that such ethics issues have been justified by additional ethics requirement and safeguard measures as … The authors assured and certified that this research has been conducted in accordance with all of the ethics standards required by the Declaration of Helsinki issued in 2013. This clinical trial has been registered in ABC with the code number 123456.

10.2. Example 2

This study is a nonexempt human research and therefore was approved by XXX-IRB on 20YY-MM-DD (COA number: ZZZZZZ). XXX-IRB is a registered and accredited IRB. The Journal identified that this study posed minimal risks to the study participants. The Journal also agreed with the XXX-IRB’s decision that the waiver of the study participants’ informed consent is ethically acceptable. The authors assured and certified that this research has been conducted in accordance with all of the ethics standards required by the Declaration of Helsinki issued in 2013.

10.3. Example 3

This study is an exempt human research in accordance with the national laws and regulations in SSS (country). The certifying letter was obtained from XXX-IRB on 20YY-MM-DD. XXX-IRB is a registered and accredited IRB. Even though this human research was exempted from IRB review, the authors assured and certified that this study has been otherwise conducted in accordance with all of the ethics standards required by the Declaration of Helsinki issued in 2013.

10.4. Example 4

This study is a nonexempt human research and therefore was approved by XXX-IRB on 20YY-MM-DD (COA number: ZZZZZZ). XXX-IRB is NOT a registered and NOT an accredited IRB. This research team has obtained the study participants’ effective informed consent prior to the outset of the research. The Journal has identified that this study posed high risks to the study participants, the Editorial Office has verified the validity of the COA and ICF via available alternative sources during the review process. Significant ethical issues have been identified as … It is reasonably believed that such ethics issues have been justified by additional ethics requirement and safeguard measures as … The authors assured and certified that this research has been conducted in accordance with all of the ethics standards required by the Declaration of Helsinki issued in 2013. This human study has not been registered in any public database.

11. Cost and benefit

In this article, AAT-ERTF proposed a flow-chart to guide peer reviewers and journal editors during review process (Fig. 1). Some elements in this flow-chart are not new, but others are newly integrated in this algorithm. The main purpose, as mentioned earlier, is to strengthen the misconduct-proof mechanism and empower the ethics culture in the academic community. When the authors are forced to fill in all the information required by the journals (e.g., context in the proposed template language), they need to and have to think over the ethics requirement and the decision whether fabrication is worthy to do. Of course, the authors still can make a forgery on the statements, but the information regarding the status of IRB, clinical trial registration, and contact information for verification purpose provides an extra layer of proof against researcher’s intention to make any misconduct.

In addition, the peer reviewers and journal editors should always keep alert during the review process to see if there are any signals as described below. A red flag should be raised if there is a positive sign of potential misconduct by the authors: (1) the authors are too prolific; (2) too productive within a short time; (3) the new investigator; (4) bad past record; (5) no clinical trial registration; (6) no citation of IRB identifier, registration, and accreditation status; (7) no detailed information regarding the COA; (8) no website to access the IRB and the institution; (9) no national or local law and regulations regarding human research protection; (10) claiming obtaining participant’s informed consent in those studies where it seemed difficult to recruit the potential participants; (11) cutting-edge research with innovative ideas; (12) high-risks human study design; (13) studies enrolling too many or too few participants; (14) no details about ethics justification or risks management plan; and (15) no response after the editorial office tried to make contact.

Perhaps some authors will see that the requirement of the proposed template language used in the Ethics statement section is an unnecessary burden to them. Perhaps journal editors will see such requirement is impractical due to space constraints in the article and costly for publication. However, it should be defended that there are < 200 words added in the Ethics statement section. In comparison to those words for disclosing a conflict of interest, fund source, or acknowledgment, a 200-words ethics statement in a published article is ethical, economical, and practical. When human research reports provide new and valid information to the academic community and the general public, the whole society and human beings get benefits. When human research conduct is ethical, there is no need to waste limited resources in investigating and correcting the misconduct and mistakes afterwards. When the publications include sufficient information on ethics issues, trust from the general public is gained. The cost/benefits ratio of such extra requirement, therefore, is balanced.

It is a collective moral obligation for all the stakeholders in human research to do everything they can to ensure the ethical culture of human research, to support good medical practice, and to produce high-quality medical sciences for mankind. The recommendations made by AAT-ERTF in this article for all involved in human research reflect this obligation.

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