Quality assurance in medical and scientific research.

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Summary.

The large literature on research misconduct is itself for the most part unscientific, so that proposals for action based upon it are unlikely to help and indeed may stifle research.

Once the real problems and failings are understood better solutions become apparent, *viz*: recognise the provisional nature of all science; make all authors responsible for the whole content of their published work; make each original paper explicitly subject to review by external assessors should concerns be raised about it in retrospect; and following that, if necessary, annotate the published work in a manner that allows every enquirer to learn its current status. In this way the scientific record would be updated and corrected where needed and made publicly available in its corrected state.

These four simple rules and procedures would strongly discourage many of the bad practices which actually do exist, expose malefactors to consequences matched to their wrongdoing, without time limit, protect the rights of the oppressed, enhance accuracy of the scientific record and render unnecessary any other methods of quality assurance.

Introduction.

There are many people in the world who doubt the conclusions of medical and scientific research, supposing that large parts of the published work are erroneous or deliberately falsified, and wish that stringent control of research should be imposed. Others desire the total destruction of science as being contrary to religion, or will follow any plausible quack whose stock in trade is 'natural' or magical remedies, or glib and attractive explanations. The common feature is failure to understand the essence of the scientific endeavour or the most elementary technology: words replace real things and then if the words of a prophet are seen as having equal value to those of the scientist, why not take the easier path and believe what is more comfortable? Thus we have a first party who seek to establish some kind of central authority that will impose the True Faith where everything in science is guaranteed, exact and certain. However, that will not placate the latter groups, and the Tridentine zeal of the first party must also do more harm than good. If there is need for Reformation, reversion to a reactionary dogma is not the way to go. This paper makes alternative proposals for change, based upon a new analysis.

A voluminous literature exists on failures of ethical conduct and quality control in medical and scientific research, much being of such deplorable quality that a comprehensive review is not warranted. Examples selected here fairly represent the genre.

Frequently mentioned is the preponderance of clinical research among cases of detected fraud[1,2]. Scientists in other fields may well resent being lumped in with the doctors but more charitable is to make allowances for the refractory nature of the subject material - human beings - and their inherent variability, so that it would be more difficult to achieve clear results in clinical research than in physical sciences even if there were no malefactors.

There is extreme variation in estimates of the frequency of misconduct, from 1:100,000 scientists per year[3], to 1% of published figures digitally enhanced[4], 7% of investigational drug trials audited by the FDA being found to have serious deficiencies[5], 13% of respondents in a survey allege having knowledge of data fabrication[6], 51% "know of at least one fraudulent project in the proximity during the last 10 years."[7], ".. other questionable practices by up to 72%."[8]. Evidently the things measured were different and no blanket statement about frequency of misconduct is worthy of comment. Survey studies might be justly be excluded as providing no evidence about actual events, but even if that is done the differences remain large, which may suggest that all chatter about high delinquency rates is a waste of time because we don't know what is meant. To understand the kind of things that really happen it is necessary to study individual cases in detail, and to estimate frequency requires a system of audit, *post hoc*.

Other disturbing features are willingness to treat subsidiary forms of publication as being of merit equal to serious academic studies[9], reckless use of language[10,11], and basing argument upon irrelevant examples[12].

There are relatively few sober and careful studies of the whole scenario, and they are all the more important for that reason. Though mentioned above, Steneck's paper (note 3) is one of those few and the only important criticism of the substance of his work is that he seeks to treat all research misconduct as distributed along a single scale whereas it seems important to examine separately the nature and impact of different kinds of misconduct, and in various circumstances. Glick[13] describes serious audit of scientific data in industrial settings and produces convincing evidence that such audit is worthwhile even if only to avoid business losses. He also provides tables showing frequency of different kinds of misconduct in research generally, agreeing broadly with the citations above - serious, deliberate, experimental fraud is quite rare, slovenly work common, and misconduct in clinical studies intermediate, though often enough it has led to criminal convictions. FDA audits have been mentioned above. Claxton (note 1) describes several of the more prominent cases of fraud and compares various studies of frequency, arriving at around 0.02% of published papers and similarly for unpublished research - but it is true that these rates are for the known cases so that they must be underestimates, and refer to outright fraud only.

Some real examples.

In recent years so much has been written about a paper by Wakefield et al[14] that it would seem odd not to discuss the case, though it is difficult because there are so many tangled strands to unpick and implications that have nothing to do with research. For the limited purposes of this article the most important things are whether the paper should have been published at all; that is, whether there was a failure of peer review, and what should have happened after that: other aspects are mentioned briefly first.

Wakefield has been struck off the Medical Register in Britain and the original paper retracted[15] and it should be made clear that neither was because of 'fraud' although that and cognate words are widely used by others[16]. The grounds for striking off can be paraphrased as:- failures in clinical ethics, concealing financial links, falsely representing the way patients were chosen for study and lack of insight into the wrongfulness and seriously adverse impact of his acts. The grounds for retraction by the journal editors were that parts of the content of the original paper were 'incorrect' and 'false' - the words falsification, falsified, fraud or fraudulent do not appear. Public condemnation of Wakefield is because of a subsequent campaign against MMR vaccination which led to a damaging fall in take-up rate, but the paper itself cannot be considered as the cause of these events, not by itself. Take for example

the completely clear disclaimer on page 641, "We did not prove an association between measles, mumps and rubella vaccine and the syndrome described." (The possibility of an association is indeed raised elsewhere in the paper, and discussed in relation to the opinions of others.) Ostensibly, the paper is an attempt to delineate a novel syndrome (constellation of symptoms and signs suggesting a disease entity) in children, in whom bowel disease occurred together with developmental regression and/or autism. Various possible pathogenic mechanisms are discussed; not MMR alone, not measles virus alone; evidence for functional vitamin B12 deficiency is considered prominently.

If everything that is now on record had been known to the reviewers, they would at least have demanded rewording at several points because the text as it stands does not correctly describe the patients, would likely have required a declaration of interest, and might also have made objections on ethical grounds. Given that they accepted the scientific content as of sufficient quality and interest to the journal's readers, there was no other reason to reject outright. In hindsight, the paper is more feeble than evil. The mention of MMR vaccine is unwarrantably strong, but is qualified by the specific statement quoted above.

There were severe adverse consequences, but not from this paper alone which must be taken in combination with other publications and public statements not examined here, and even then blame falls at least equally on the ignorance and anti-scientific attitudes of the public, including the most sophisticated, who accepted the cheap, journalistic interpretation that a non-natural, medical intervention (MMR vaccination) had now been proved to be harmful by a sole crusader fighting alone against the establishment. Second, peer review never was and never can be an authoritarian system for preventing publication of improper material. Third, Wakefield had prior, published work suggesting that persistent measles virus might cause bowel disease[17] - suspect now perhaps, but at the time it looked interesting. Fourth, whatever happened to free speech? Another Wakefield should properly be allowed to publish his results and views, unless serious inadequacies are detected at the time, and it is for others to show why he is wrong. In the Wakefield case itself this has been done, though it took a long time.

What is now known was not known at the time and could not have been found out by any reasonable allocation of resources. Rather than an important example of fraud in clinical research or evidence that approval by an Inquisition should be required before each paper is published, the Wakefield debacle argues rather for rapid and sharp post-publication review. If that had been made easy in the manner proposed later in this paper, with the authors contracted to cooperate as the price of reputation, the criticisms that later emerged could have been made available at once to the editor and instead of appearing as petty complaints by adversaries could have resulted in the paper being marked as unreliable within weeks of its first appearance. Suppose anyone had simply written to say that these were not consecutive patients presenting independently to the clinic, or lumbar punctures were done without clinical justification, or Dr Wakefield was in contact with lawyers about possible MMR lawsuits, what could the authors have said in rebuttal?

In contrast to that drawn-out nightmare, when serious scientists are challenged about the validity of work from their own units their response is often quick and thorough. Such people care about both the truth and their reputations.

[18]Mark Spector used sophisticated, fake laboratory procedures (parallel to and replacing the designed experiments) giving images that might not have been questioned for years but for someone's chance observation that radiation had passed through a glass sheet. That very sharp observer also knew enough to understand that therefore the source could not be ^{32}P which would have been used in the proper experiment. Spector used ^{131}I, giving more penetrating and longer-lasting radiation. An arrogant choice; he must have thought no-one

would ever check, because he knew the right answer in advance so there would be no need to check, and to promote his own advantage all he had to do was produce something that looked like the expected experimental result.

Several similar cases are described by Claxton (note 1) and retractions appear from time in the most prominent journals. Nowadays this will usually be after an institutional review has allocated blame, and in cases where the culprit chooses to deny wrongdoing the process is much prolonged because overwhelming evidence is required on every tiny detail for fear of a legal counterblast by the accused person. An easier, quicker and fairer way is outlined later in this paper and, as Fanelli[19] points out, these retractions show integrity of the scientific enterprise as a whole, not only the error or malfeasance by individuals.

What has been done about research misconduct, or is proposed by others.

- Enhancement or refinement of the peer review process, it seems amounting almost to censorship and based on a misunderstanding of what peer review is about.

- 'Retraction' of papers held to be affected by fraud or misconduct of researchers, and in lesser cases publication of corrections in a later issue of the same journal - though this latter is usually about misprints or other editorial errors rather than scientific substance. The meaning of the word itself deserves closer scrutiny.

- Authors are required by some journals to give much more detail than before about who did what, who has any possible financial interest in the outcome and who guarantees the work. Morally this is clearly a Good Thing, though there are aesthetic objections.

- Ethical control, extending to approval of the design of experiments. This applies in the first place to work involving human or animal subjects, but some seem to wish that it may be extended, as appears next.

- A Concordat of research institutions and publishers in the UK to establish a system for preventing false publication before it happens, of which the following give only a pale reflection of the whole: 'institutions must have strict and robust protocols in place for investigating misconduct allegations', 'It is the employer's responsibility to orchestrate confidential investigations …. adequate mentoring', 'confidential third party … whistleblowers, ', 'imposing of sanctions and reporting to regulatory and statutory bodies, funders and researchers', 'comprehensive national framework', 'research integrity officer, 'register with a national advisory and oversight body', 'Major grant-giving bodies such as the Wellcome Trust, …. have also confirmed that they would be incorporating the concordat's principles … ', 'surveillance of research misconduct', 'adherence to agreed protocols', etc.[20].

What may be objected to those actions and proposals.

Concerning the Concordat, note the corollaries that research will have to be done in **institutions** which must be **registered** with a governmental body or quango, by **employees**, under **management** which includes a research integrity officer, conducts surveillance and mentoring, orchestrates confidential investigations and imposes sanctions, and all this so as to do experiments according to **agreed protocols**, which evidently must be set by some higher authority. The whole thing is a Blairite, *quasi*-fascist nightmare.

Is there any evidence that this kind of regulation works? Our beloved Care Quality Commission for example? And who will be that higher authority; the Group Leader, Head of Department, Vice-President for Research, Chairman of the Board, Prime Minister, God?

And it cannot possibly work. Even if research is regulated by the highest in the land, fraud will continue to be done by individuals who think that truth doesn't matter and they can get away with it; and who will in the short term because it isn't difficult to do and may not be noticed at all if your 'experimental results' were correctly guessed (dodgy dossiers, anyone?). The more elaborate a system of control, the more it will encourage conformist fraudsters publishing incremental *pseudo*-research, who will only be caught out if the truth is different from expectation so that the fraudulent claims are finally shown to be wrong by exposure to the light, and then only if they are important enough to be worth the bother. Most fraudsters detected to date, like Spector (note 18), were intellectually arrogant, supposing that that they knew the answers already so that experiments were only confirmatory. In a less prominent field with a less ethical boss, he might never have been exposed.

And it will destroy the thing it seeks to regulate. Stable doors, babies and bathwater, geese and golden eggs spring to mind. The system and style of control proposed must stifle creativity and science is nothing if it is not original, the product of enquiring, independent, creative minds.

And it isn't necessary, partly because the situation has been misrepresented, and even if it were as bad as some people think there are much, much easier ways of ensuring quality.

The scientific enterprise and the range of things that can go wrong.

If it is fair to criticise the scientific endeavour it must be equally fair to respond and put forward completely different views of the situation and what should be done. For those predisposed to suspicion, the literature accounts of research misconduct may indeed sound alarming, even if less so than the diagnoses and the prescriptions for treatment - atavistic reactions based on scant evidence. From a less paranoid standpoint it remains true that this is a human enterprise and therefore things can go wrong, including some not often mentioned though perhaps more important than those which dominate accounts of the subject.

The following list is in a tentative, approximate, increasing order of blackness in the catalogue of evil. An offending piece of work should be placed in the highest applicable category; for instance, just because a paper is trivial or obscurely worded does not stop it being also fraudulent. Publishing too much features in the first four and publishing too little in the next two: in general, a lot of stuff gets published that shouldn't be, and *vice versa*, but these are not the most important things.

1] Vanity aside, there is a wholly honourable pressure to publish because otherwise the world will never know, and added to that is the drive for priority. These may lead to work being released that a modest author, in retrospect, will regret.

2] Career advancement depends upon publication record (including impact factor of the journals concerned) which is used in assessments for appointment, promotion, allocation of research monies and ranking of a department, unit or university; so the decision to publish is now influenced more than ever before by frankly venal considerations.

3] Double publication.

4] Trivial publication, exaggeration, obfuscation (what cannot be understood is difficult to criticise).

5] Timidity; failure to submit material that should be published. Unintentional influence of authority, implicit bullying inhibiting publication, might rank here or higher.

6] Surely, if humans have been at any risk the results should be publicly available so as to reduce the risks for those who come after, whereas this is done for only a minority of clinical trials; because of commercial interest, which may also block publication of other kinds of work.

7] Guest authorship.

8] Plagiarism: failure to attribute: theft of ideas.

9] Ethics: not paying attention to other ethical matters or an Ethics Committee.

10] Failures of peer review, leading to publication of plagiarised, inadequate or obviously incorrect papers that might properly have been excluded; and citation by authors of discredited research as if it were reliable (because that is something capable of detection and correction upon review). Included at this level also is a reviewer's innocent rejection of valuable work.

11] Error; more importantly not taking vigorous action to correct error or diminish its effects as soon as it is detected. Not checking validity of methods. Self-delusion is ranked here, as a species of error rather than a greater evil.

12] Failure to protect whistle-blowers, the whistle-blown, honest mavericks, and against bullies.

13] Fraud: inventing, concealing or misrepresenting results; or a reviewer who allows personal interest to bias conclusions, or steals priority. (The word 'fraud' is used here as shorthand, ignoring the strict legal meaning.)

14] Misleading publication supporting commercial or political interests. There are even scientific-looking journals nowadays which exist only to tell lies on behalf of their paymasters. Much advertising should be included here, in the lowest circle of hell.

A case described by Glick (Note 13) is illuminating as a stress test of the above tentative classification. Company employees slanted their report of experimental findings towards what they thought their managers wanted to see, and this was detected on audit. Those managers in turn had no interest in truth or falsity, wishing only to impress more senior management. The scientific record generally is not affected by behaviour of this kind (if confined within the corporation) which arises from relationships in the organisation amounting to implied bullying or even overt bullying. However, the scientific workers concerned did misrepresent their results and presumably this has to be classified under number 13 or 14. It seems hard that they should be thought guilty of worse misconduct than the managers who were felt to have pressured them into it - perhaps it should be number 14 for all of them? But how do we punish those non-scientist managers, who were only behaving according to their own professional norm of perfect selfishness? Do they go free?

Priority, Invention and Ownership.

These things deserve a few words without implications about wrongdoing because they do influence people's conduct. In normal science, from the time of the early Royal Society (so for some 350 years), priority has been credited to the first to publish: dates of the original work and of submission for review are not counted. Contrariwise, from the very beginning of patents for inventions priority has been for the first to file a patent application and everything else is irrelevant (except in the USA where special rules apply if the original work was actually done in that country and can be dated). When acknowledging inventors US patent law again differs from other countries - the actual inventors must be named rather than only the legal owner of the rights to exploitation. The US practice seems preferable.

Research misconduct in its setting.

If an individual scientist is found responsible for any of the more serious failings listed above (say, those from number 3 onwards), presumably everyone agrees that if a punishment can be arranged that will fit the crime, it should be imposed. But that leads to new problems, namely how to attribute responsibility, precisely, down to the level of the individual, and what punishment is fitting in each particular case. It is true that any

misconduct no matter how slight sullies the scientific record to some degree, but it is proper also to ask, how heinous?, and whether a particular occurrence has any significance outside the profession of Science, and whether that should influence the course of action to be taken. In any system of justice societal norms influence the nature of punishments and cannot be ignored just because we are dealing with an area where particularly high standards are demanded. We no longer hang sheep-stealers, or even murderers.

Science versus the scientist.

In the long term, for the world at large, there are things more important than the conduct and punishment of an individual scientist, namely that the scientific enterprise should be unimpeded, the scientific record should not be significantly damaged and if such damage has occurred, that it is corrected. From this point of view, punishment of the errant individual is a side-issue, a red herring, what matters more is the scientific record and an important corollary is how to prevent the continued influence of discredited publications. These considerations rather than a concentration on purity and ill conduct of individuals are what should guide plans for change.

In case any reader thinks that the writer's attitude is one of denial or overly lenient, let me say here that I have personal experience of misconduct falling under numbers 4, 5, 8, 10, 11, 12 and 14 of the above list, did some whistleblowing of my own, resent being involved in any of it, before the key events and even more so after have been sensitive about 'ownership' of intellectual work and if there had existed at the relevant times a remedial process capable of swift, fair consideration and proportionate response would certainly have made use of it. But none of those occurrences have had the slightest influence on the progress of science, and no-one now will want to hear about things that really don't matter anymore.

Quality assurance in science. 1] The published record.

Original scientific research is not like manufacturing industry. The product, even after it has been published, is not a finished thing but at best a prototype, subject to revision and improvement, quite possibly to be abandoned as unprofitable or mistaken. It follows that quality assurance cannot be of the same kind as in industry and that it can and should be undertaken after publication, whatever may also be done before. The starting point is Ten Commandments of scientific publication of which the first four may be thought to summarise the whole present approach since the others and also the subsequent proposals for action can be seen as consequential upon them, to expound, expand and explain in more detail.

I All scientific results and conclusions are provisional; all may be questioned, corrected and enlarged upon without necessarily any attribution of fault.
II All authors equally bear responsibility for the whole of the published work.
III All authors must agree in advance, as a condition of being published, that their work may be scrutinised by others after publication and they will provide whatever further evidence is called for in such a case and cannot object to annotation of the published paper.
IV All published work may be annotated by authority of the Editor to show the current state of knowledge and opinion about its accuracy and merit.
V Only those who did the work, and all of them, have the right to be recognised as either authors or contributors, including those who provided only ideas. This applies whatever rights have been assigned to other parties. Non-listing of a contributor may be corrected in retrospect by annotation of the published work without necessarily any implications.

VI However, no-one has the right to prevent or inhibit publication: thus work may be published without the consent of all those entitled to be named as contributors.
VII The authors jointly may 'withdraw' the whole of the work, or annotate the work, whenever they wish if the ground is that some flaw has been found, but not otherwise.
VIII In the same way, and only on the same ground, any author or authors may annotate the work without all authors agreeing to the action.
IX Published work may be annotated without consent of the authors if significant failings are found to exist, or additional evidence is requested but not provided or is unsatisfactory, or to correct the list of contributors, or if evidence is found of bad treatment of any individual.
X Work that has been annotated or even formally 'withdrawn' will not be deleted but appropriate labels will be attached to advise anyone who accesses the publication, and the existence of labels must be made known in any review or commentary referring to the work.

Many things follow from the Commandments, as will be obvious to any reader, but they do not include a free-for-all because there will still be an editor or someone very like that acting as a referee in the case of disagreements which is pretty much what editors do now in like case; receiving complaints, deciding whether there is *prima facie* evidence and investigating as necessary. A distinction is drawn between authors and contributors, but this is not necessarily adverse for a contributor. The Commandments refer to formal scientific publication and if material is published in other ways it will, as now, lack the corresponding cachet. The immediate and potentially severe penalty for misbehaviour over publication is loss of reputation and the IIIrd Commandment makes it rather easy to proceed against anyone. If questions are raised about validity of results or conclusions, authors may well choose to mitigate the consequences by voluntary retraction or annotation. It seems likely that this would become much more common and more rapid than at present, since in many cases a full enquiry would not be necessary - no Research Integrity Office, no *quasi*-legal process, simply the editor writing to any one of the authors to say, "Please show me the original gels and notebooks", with annotation to follow if the authors find themselves unable to respond fully.

Quality assurance in science. 2] The proper conduct of research.

Is it possible to establish a related set of rules for doing the research itself? The answer must depend on our understanding of what science really is so a founding definition or axiom is required.

Definition. "Scientific research consists of making observations, leading to new ideas about the real world that are then tested by experiments which must include the possibility of showing that the hypotheses are wrong."

Practice. The first two things in the definition cannot be made to happen in a pre-determined way though certainly some preparedness is possible. Concerning the third, it is proper to emphasise rigorous experiments leading to definite conclusions, though it will be better in the long run if the design can also be such that novel observations are possible leading to a new round of hypotheses. Therein lies the art of experimentation ("Never do the first experiment too carefully", an epigram attributed to A.J.P. Martin, or my own counsel to research students, "Never do experiments: you don't know what you might find"). No more detailed statement can be made about scientific research without first specifying which area of science in under discussion.

Morality of scientific research. There is an unambiguous moral objective for which no apology need be made - the acquisition of correct knowledge of the real world.

Morality of medical research. Some think that medical research needs to be justified by appeal to usefulness and the greater good of mankind[21], but that is really about the moral commitment of Medicine rather than the research.

Bias. Prejudice and bias are ever-present and all researchers should be alive to the possibilities. Commercial bias is the easiest to recognise and obviate.

Law. If research is done in a manner contrary to law, those who do it must expect to bear the consequences. Sometimes *samizdat* research may seem to be morally necessary and if successful should be published whatever sensibilities it may offend: that makes no difference to the applicability of Law.

Ethics. There is no question that research in which humans or animals might be harmed must be subject to ethical rules and something very like Ethics Committees must continue to exist. But such bodies should not be in a position to prohibit research; their performance has commonly been poor and it is simply not true that there is uniformity of opinion even among professional ethicists about what should and what should not be approved. A solitary example will suffice[22].

Clinical trials. However much drug firms may protest about commercial confidentiality, it seems morally clear that all clinical trials should be registered and their results made available publicly in a manner that might differ in detail from formal scientific publication of other kinds, though the principles must be the same. Legislation will be required including provision to bring international corporations into line by making all marketing authorisations and patent rights dependent on the owner being fully compliant.

Whistleblowers. Much is made of whistleblowers, their value to science, their hard life and the need to protect them. My personal experience is supportive of these propositions, but the real situation is extremely complex and goes far beyond the popular conception of a lone prophet preaching in the wilderness. Practical proposals are made below.

Finance and control. Funding of research is with those who have money to spend; chiefly governments, the great research charities and corporations; who will make their own rules about what they will pay for and how it should be done. There is no legal compulsion on them to honour the principles of science (it is surprising how often they do given the pressures upon them) and no reason either to give their policies the dignity of moral imperatives. For example, if a donor requires that a clinical trial must have Ethics Committee approval before it begins, that becomes a contractual obligation under civil law which can easily be made to have civil penalties attached, and that should be sufficient.

Quality assurance in science. 3] Practical proposals, and consequences.

Responsibility for science should be placed where it belongs, on the individual researcher and author, which leads to proposals of which some may be already well accepted, or resemble what is presently happening (without acceptance of the personal responsibility requirement).

Ethical approval and clinical trials. These are discussed sufficiently above.

Peer review. Both work for publication and grant applications should be reviewed for quality, as now, and reviewers should be required to take responsibility for the probity of their work. However, peer review cannot be a guarantee of accuracy or scientific merit. Any attempt to make it into a means of censorship and control of what science may be done or reported is not only doomed to failure but is also contrary to scientific morality and should be rejected with contempt. If an editor or reviewer misses serious flaws it may be a matter for commiseration from his colleagues, or criticism in respect of want of care or knowledge, but

it is not the journal's business to repeat the actual experiments that were done (or not done, as the case may be); only to judge the quality of what is described.

All papers must be capable of annotation or outright retraction. This recognises the essentially provisional nature of all scientific findings and will make it easier to correct error, punish wrongdoing proportionately and protect those accused of misconduct. Proportionality of response will allow better and quicker decisions, which may include overruling a decision previously made because it is later found to be too harsh or too lenient. In practice it seems that this will require all original scientific publication to be in electronic format, with prior agreement that the publishing authority (the 'journal') may investigate circumstances brought to its attention and then annotate the document in a way that will be seen by anyone who accesses it, leaving the original text available for comparison with any amended or annotated version. More difficult to implement but of nearly equal importance, such annotation should be updated automatically in articles commenting upon the original work.

Something of the sort is already happening in the blogosphere, but that is ephemeral and needs to be clarified and fortified in the manner described.

Some desired consequences.

The 100-author paper, guest, ghost, uninvited and undeserved authorship will disappear. No-one will dare to be named as an author without access to the experimental records and full understanding of the work. Modern methods of sharing and archiving data make the process of review and annotation relatively simple and fair. A corporate body that wishes to conceal who did what cannot also claim the cachet of science. Contributions other than authorship will be listed as such and few will dare to conceal any significant outside influence.

It is essential that annotations should be available to any searcher, from which it seems to follow that all publications should be electronic and available publicly free of charge complete with annotations, removing a current impediment affecting those without funds to pay for access. Much of the literature is already free on the internet but a greater quantity is charged for or becomes free only some months after the original publication date and there are many poorly-funded institutions which cannot afford journals[23].

Will the journal editor survive? Editorship has always been a position of pride more than of financial reward and it will probably be advantageous to retain the prestige of each publishing organisation so that editorial staff will wish to work there and authors prefer to have their papers published by one rather than another.

Impact factor would then continue to exist with its advantages of encouraging competition both by the publishing organisations with each other and by scientists, although there may be also potential disadvantages[24].

Some undesired consequences.

There are ethical commercial publishers and learned societies that depend on journal subscriptions and whom we all wish to continue. Then must authors all pay for publication? Page charges already exist for some journals and bear unfairly on those who lack funding so the problem is already well known. Possible solutions surely exist.

Will the print journal survive? Perhaps, in much modified form and containing only commentary articles. Much essential content is already buried in electronic 'Supplementary Information' or papers are published only in electronic format, so what is proposed is already half done and at most will accelerate a work in progress, though with broader objectives.

The nature of annotations.

It will not be necessary to spell out every possibility and they will vary from condemnation though implied rebuke to exoneration. Examples:

"The authors have not produced the original records requested and therefore Figure 1 is to be regarded with reserve unless and until the observations can be confirmed."
"It now appears that the paper does not contain new material sufficient to justify publication. The experiments described closely resemble those of Hobson and Jobson published in *Genesis*, Book 75 (1000 BCE) verse 93, which was not cited among the references."
"The authors wish to retract the paper in its entirety, though reserving the right to submit further material on the same subject after completing new experiments."
"It has been brought to our attention that John X contributed significantly to the statistical analysis. We apologise to him and his name is hereby added to the listed contributors."
"Criticisms made by Jane Doe of the experiments described in Figure 2 have been evaluated by the undersigned who have had access to primary experimental records including the original gel that is illustrated. We conclude that Ms Doe's criticisms are unfounded."

W*histleblowing and related matters*.

A whistleblower's complaints should receive attention; so also should the response of those accused of misconduct; it is not a one-way trade. The proposals put forward here will make it easier to be fair to both sides and clarify the record in respect of either false or mistaken statements or unjustified suspicion - though the process can only begin after publication. What has not yet been published cannot be judged by outsiders and is not the concern of the scientific community as a whole, nor the public, though it may well be for an employer and appropriate control structures can certainly be made a condition of the award of a research grant. If a whistleblower has information, let it be produced when the authors have committed themselves, by publishing, to the evidence upon which they rely. Contrary evidence cannot be judged until we know what it is contrary to. The authors can then be invited to respond, conclusions reached and the appropriate action taken which, as has been hinted above, may not always suit the complainant.

Anonymous complaints are usually incapable of analysis because it is necessary to know the circumstances under which observations of misconduct took place.

It is not possible to protect either whistleblowers or those whom they accuse from all unintended consequences. Suppose a complaint is indeed made anonymously, it will often appear obvious who made the complaint. Whether or not anonymously, it may well be that a complainant soon feels that his or her position in the organisation or in relationships with colleagues has become personally intolerable, forcing a move of job, house, city, country which may or may not turn out well, may make or destroy a scientific career. Whatever help is promised or really provided the upshot is unpredictable simply because some consequences of a whistleblowing act, by their very nature, cannot be under the control of any authority. On the other hand, if post-publication review and annotation become widely accepted, successful whistleblowers may sometimes find their careers enhanced.

Whatever is said about whistleblowers applies equally to the objects of complaint (here called the whistleblown) and to those who wish to do research or publish on subjects outside the main stream - the mavericks. We should do whatever can be done to protect their interests and rights too, but we cannot prevent unfairness at all times and in all places. The most important help that can be given is to let what is said and done be public.

Bullying.

In the above list of kinds of misconduct, [5] includes what may be called covert or unintended bullying. Without having any formal power, a Head of Department or research group leader has influence on juniors' careers which may be favourable or otherwise, for various reasons: because it is the custom in life and business generally; people seek his or her opinion; and there has been in the scientific community an understanding that a whole area of

research in some sense 'belongs' to its originator. Even Watson and Crick are thought of by some as interlopers. So authorship is given to those who do not deserve it or publication is deferred until the perceived authority figure is dead and can do no more harm.

Overt bullying (Item 12) is less common in normal science, perhaps more so inside corporations as discussed above, but it does occur and can only be resolved if there is a mechanism by which a higher power takes over management of the particular employee or individual from the bully. The same might be said of whistleblowing, but then the original complaint may appear to be against a whole organisation rather than one malign person, making any kind of constructive response more difficult.

Punishment that fits the crime.

It is hard to imagine a heavier punishment than being obliged to retract published work or have it effectively cancelled by the editor; and that is the appropriate consequence for sloppy, erroneous or fraudulent work. Partial mitigation can be achieved through prompt, vigorous investigation by the original authors to establish what went wrong - exactly the response of serious scientists as mentioned earlier (references, notes 1 and 18) from which we may justly deduce that anything less is suspicious.

It will be clear that lesser degrees of fault could be readily dealt with by lesser degrees of corrective action - apology, amendment, explanation, partial retraction. Each such step would alleviate personal slight or hurt as well as correcting the formal record because each step would involve naming those involved on both sides.

How quick? It is hard to imagine such an investigation and judgment taking more than six months because it would be in the interests of all parties to finish quickly. Failure to cooperate or answer questions quickly would of course be taken adversely and this would be provided for by formal agreement prior to publication.

Conclusions:

Science and scientific research are not creatures of government or corporations, not dependent on the will of politicians or boards of control, but spring from the individual human brain and the society within which it operates. Accordingly, they cannot be controlled or perfected by law or management decree, so that previous proposals for reform are to that extent wrong-headed. As in any human enterprise there will be fallible scientists and failures in science that cannot be prevented absolutely: therefore the scientific record should be made capable of annotation after publication in such a way that all forms of misconduct or error are discouraged, made known, and consequent falsities corrected in such a way that the facts can be seen by everyone, for the benefit of science, other scientists and the people at large.

Notes and References:

[1] Claxton LD. Scientific authorship Part 1. A window into scientific fraud? *Mutation Research* 2005; 589: 17 – 30. Page 24, "In the biological sciences, most known cases of fraud and other types of misconduct have occurred in biomedical (mainly clinical) research."

[2] Fanelli D. *PLOS One* 2009; DOI: 10.1371/journal.pone.0005738. Page 8/12, "samples drawn exclusively from medical (including clinical and pharmacological) research reported misconduct more frequently than respondents in other fields"

[3] Steneck NH. Fostering Integrity in Research: Definitions, Current Knowledge, and Future Directions. *Science and Engineering Ethics* 2006; 12: 53 – 74, page 57.

[4] Steneck *op cit* page 58. The author cites Rossner (2004, a conference presentation) but the web page cited was not available when access was attempted. For reference see note 3.

[5] Claxton *op cit* page 23. For reference see note 1.

[6] Khajuria A and Agha R. Fraud in scientific research – birth of the Concordat to uphold research integrity in the United Kingdom. *JRSM* 2014; 107: 61 – 65. Their reference 28 (authenticated) is to a news article and it is mis-quoted. The actual original wording is, "inappropriately adjusting, excluding, altering or fabricating data".

[7] Ranstam J, Buyse M, George SL, et al. Fraud in Medical Research: An International Survey of Biostatisticians. *Controlled Clinic Trials* 2000; 21: 415-27. This survey was conducted among its members by the International Society of Clinical Biostatistics. Even so only 37% (n = 163) responded, of whom 51% did so as quoted in text and 13% "have been requested to support fraud."

[8] Fanelli *op cit* page 1/12 (Abstract). For reference see note 2.

[9] See Note 6 for one example. Another is in Fanelli *op cit* (note 2) where on page 2/12 Steneck *op cit* (note 3) is cited for the fraud rate of 1:100,000 scientists, followed by, "or 1 every 10,000 according to a different counting", citing a news article that does not state how its figures were arrived at and where '10,000' may well be a misprint.

[10] Ioannidis JPA. Why Most Published Research Findings Are False. *PLOS Medicine* 2005; DOI: 10.1371/journal.pmed.0020124. Notwithstanding its title, the paper is a discussion of the statistics underlying clinical-medical research, not research in general, and the likelihood that a small effect may be exaggerated or annulled by a small observer bias. There is nothing about any actual research project and the conclusions may seem obvious.

[11] Godlee F, Smith R and Marcovich H. Wakefield's article linking MMR vaccine and autism was fraudulent. *BMJ* 2011; 342: 64-5 c7452. On page 65 the following appears, "The Office of Research Integrity in the United States defines fraud as fabrication, falsification, or plagiarism." But that is wrong: the quotation is from the ORI definition of misconduct, not fraud: they are different words with different meanings. Khajuria and Agha (*op cit*) misquote or exaggerate at several other points, not only as cited in Note 6.

[12] Fanelli *op cit* (reference note 2). This paper is essentially a meta-analysis (of survey studies), but also cites at least one news item as mentioned in note 9. Steneck *op cit* (note 3). Discussion on page 58 and references 18 to 21 relate to academic misconduct rates among undergraduate engineering, medical and nursing students, and in 'honor-code schools' - populations which have nothing to do with scientific research.

[13] Glick JL. Scientific Data Audit – A Key Management Tool. *Accountability in Research* 1992; 2: 153 – 168.

[14] Wakefield AJ, Murch SH, Anthony A, et al. Ileal-lymphoid-nodular hyperplasia, non-specific colitis, and pervasive developmental disorder in children. *Lancet* 1998; 351: 637-41.

[15] The Editors of The Lancet. *Lancet* 2010; 375: 445

[16] Khajuria A and Agha R *op cit* (note 6), Godlee *et al*, *op cit* (note 11).

[17] Wakefield AJ, Pittilo RM, Sim R, et al. Evidence of Persistent Measles Virus Infection in Crohn's Disease. *Journal of Medical Virology* 1993; 39: 345-53.

[18] Racker E. A view of misconduct in science. *Nature* 1989; 339: 91-3.

[19] Fanelli D. Rise in retractions is a signal of integrity. *Nature* 2014; 505: 33

[20] Khajuria A and Agha R *op cit* (note 6), pages 62-63.

[21] Oakley GP and Johnson RB. Balancing benefits and harms in public health prevention programmes mandated by governments. *BMJ* 2004: 329: 41-3.

[22] Shaw D. The right to participate in high-risk research. *Lancet* 2014; 383: 1009-11.

[23] Kebede D, Zielinski C, Mbondji PE et al. Institutional facilities in national health research systems in sub-Saharan African countries: results of a questionnaire-based survey. *JRSM* 2014; 107 (IS): 96-104. The paper describes results of a questionnaire survey of health research institutions in sub-Saharan Africa. On average, respondent institutions subscribed to 3 electronic journals: the average number of print journals is not stated.

[24] Schekman R. How journals like Nature, Cell and Science are damaging science. *The Guardian* 2013, December 9th. He comments favourably also on the quality of open-access online publication systems.