

October 2024

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1. Background

Context

The following is prepared 4 Oct for [REDACTED]. It is based on what I sent at the request of the Senate Clerk (Feb 2023) who promised that she would forward it to all Hawaii Senators, with no response from them to date. It is also based on correspondence (Sept 2022) with Deputy AG Diane Taira who neither accepted, closed, nor actively pursued the issue, she ended with “Sorry to have taken time to respond. We’re slammed here! “ Finally, it is based on my input to a project by a consortium of the schools of public health (Columbia Univ, NYU, Syracuse and Ohio State’s) called “At the Crossroads of Pandemic Inequity and the Backlash Against Public Health” (Dec 2023). This project describes problems/solutions encountered by US government health authorities during the COVID outbreak.

I have also contacted many public and private agencies to address this matter and their responses to not resolve (or delay) now threatens US medicine and public health. In my effort to describe my predicament and argue my innocence I have come to realize that I am a Whistleblower claiming that others (Hawaii State Legislators and their media collaborators) have violated two important federal rules.

I will assume that there is to be no retaliation against whistleblowers if claims are made in good faith, whether they are eventually proven to be right or wrong. I feel that I am right, having taught and practiced these principles for decades, and have yet to hear valid scientific rebuttal by legislators/media (beyond their personal attacks). Without a quick honest resolution, this issue threatens the ethics, processes and rules of medical science. Ultimately medicine will suffer. Beyond the threat to medicine, legal and political institutions will and should suffer for

weaponizing such important principles, applying them arbitrarily and capriciously for political or personal reasons.

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Hawaii State Department of Health
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1985-2005: Walter Reed Inst of Research and World Health Organization (WHO)
2013-2019: Advisor to US Congress Medical Research Program

History

Like the many national and international committees that I have served on for decades (WHO, US Congress Medical Research Programs Doctors without Borders (DNDI Section)) at each session we open with a thorough review of the concept of conflicts of interest. How they might affect our opinions and subsequent actions. This was noticeably lacking at all sessions convened by my detractors (Hawaii legislators, Hawaii Medical Review Board?, Social Media). In fact, they often resort to arguments quite contrary, stressing input from “stakeholders”.

Conflicts of Interest

The medical community has identified, then tried to address widespread conflict of interest (COI) in regulators making health policies. While some may justify their actions as motives of good faith, free speech or due diligence, the position of the Institute of Medicine (IOM) cited by Steinbrook in the New England Journal of Medicine (NEJM) in 2009 cannot be ignored. Furthermore, it was a response to an earlier study (NEJM 2005) that showed senior regulators could not control COI despite their own claims to the contrary.

NEJM 2009: <https://www.nejm.org/doi/full/10.1056/nejmp0810200>

“...a set of circumstances that creates a risk that professional judgment or actions regarding a primary interest will be unduly influenced by a secondary interest.” The primary interests of concern include “promoting and protecting the integrity of research, the welfare of patients, and the quality of medical education.” Secondary interests “may include not only financial gain but also the desire for professional advancement, recognition for personal achievement, and favors to friends and family or to students and colleagues.” Of course, public attention has focused primarily on financial conflicts of interest, and the IOM did so as well, viewing them as “not . . . necessarily more corrupting” than other secondary interests but “relatively more objective, fungible and quantifiable” and “more effectively and fairly regulated.”

Again, the above 2009 IOM position was taken partly in response to senior regulators either deluding themselves or lying that they could control their own COI, Steinbrook in 2005:

<https://www.nejm.org/doi/full/10.1056/nejmp058108>

While I do not expect non-physicians to have considered the above ethical issues well enough for self-reflection, I do expect agreement that they are important factors influencing everyone's positions, especially when not disclosed. And I ask for written disclosure of all involved. Most worrisome are the touted "collegial" nature of relationships among legislators. Can they fairly respect opinions of others outside of their "ohana". As in my case, will they even listen?

To the above IOM principles I have voiced my own concern, the darker mirror image to enticements. The threatening "stick" as an alternative to the enticing "carrot". The threat (fear of retaliation) can also bias one's position away from truthfulness. Many of my fellow physicians told me in private that they agree with my COVID positions – but that they would not go public with their support for fear of also being labelled disseminators of COVID misinformation. Indeed, until I was cleared of misinformation allegations, I (under the advice of legal advisors) chose to limit my comments from what I knew to be the "whole truth". A position I have never done in my 45-year career in medicine. This trend among upright doctors, who shun enticements but still can be threatened, has already begun to damage the scientific aspect of medicine in our society. Silenced physicians come across as apathetic or "burned out" post COVID, when in fact many continue to live under implicit threats of a bullying authority. Time will not and should not heal this wound, it only festers.

For the record, I want to state that I have no enticing conflicts of interest to myself, friends, students or colleagues. But I do live under an unresolved threat (re-surfacing in court by AG lawyers in 2023, when I spoke as an expert witness on an unrelated issue). And those who continue to threaten me are themselves, ironically, violating Federal rules. Furthermore, I have an unresolved 20 year old complaint against a federal office (Office of Human Research Protection) for not sanctioning the University of Hawaii ethics review board (IRB) for falsely, publicly, accusing me of cheating as a researcher. This issue was partially resolved through settlement against the former of IRB Chair (Bill Dendle) personally apologizing, but never officially in his role as the committee chair. I can see where I might have a "trouble" maker label – but it is only among collegial bullies and those who want to cover-up that their way of doing business is a federal violation, which has reached the tipping point of threatening medicine in our society.

The Violations

In the fall of 2021, the Hawaii Legislature publicly called for (in a public Senate Video) and signed a document to remove my medical license and for me to be fired from my state job as Medical Officer of Maui County. The video went viral internationally. The specific allegation was my discussing off-label COVID drugs for early treatment. Initially the accusation included being anti-vaccine until it was realized that I had sponsored thousands of COVID vaccinations on Maui. Eventually I cleared my name with the State Licensing Board, gave two hour long AKAKU

(Maui Public Television) presentation on the science of my position, and published comments on this topic in the Journal of the American Medical Association (JAMA). Many doctors are now afraid this will happen to them as many drugs currently prescribed (20-30%) are in off-label status. As federal authorities attempt set up regulatory agencies for “controlling” medical misinformation, will they overreach into off-label rules as they have done to me?

The Hawaii State Legislature has violated (at least) two federal rules. The False Claims Act (FCA) pertains to making claims about drugs still under off-label treatment status. In hindsight, premature claims may turn out to be true or false, but violators are still sanctioned for making claims before the studies for safety and efficacy are completed, analyzed, reported and openly discussed. Discussions to influence drugs still in off-label status are the realm of only licensed doctors, with significant (millions/billions of dollars) fines for violations by non-doctors, usually for promoting use of these drugs before they attain approved status. In my case legislators made false claims to block "competitor" drugs (Ivermectin and Chloroquine) still under off labels status. In my three decades of work with US and international regulators, this type of “blocking” effort is very damaging - just not so apparent to those outside of the regulatory world. During the pandemic I am not surprised that those with huge conflicts of interest (as defined by the IOM) have adopted this strategy to block the “competition” drugs for early COVID treatment. The stakes outlined by the IOM were huge. Other non-physicians were also wrong to promote these drugs. It does not matter what side of the argument one takes (I gave both pros and cons); non-physicians do not enter public discussions to influence their use., directly or through the media. Once the “old-drug-against-new -disease” studies are completed then anyone can promote or block a drug – BUT they now have to align with the position of the FDA who now approve/or disapprove a once off-label drug against the new target disease.

The second violation has to do with the long standing federal DHHS rule that clinical experiments (off-label drug status or not) must have their results for safety and effectiveness accurately (scientifically) analyzed and reported. Once reported, the observations are open to peer reviewed “discussion” with the journal editor often facilitating back and forth published positions by credentialed readers. For COVID, besides off-label treatment, I also entered into key published forums for topics including airport testing and effectiveness of masks. For the first topic we submitted an original article to which comments followed. We were requested by the editor to then write the review article for the topic. All of this and more in published, editor and peer reviewed journals, vetting our credentials and conflicts of interest.

This is no different than the principle of timely reports of results for, say, cancer clinical trials. This would mean reviewing the science of: study design, monitoring, data collection/analysis, validation of results/conclusions (involving peers reviews) disseminations of results and addressing valid feedback to such reports. Participants in these processes first declare their conflicts of interest and if judged to have too great a potential for bias must recuse themselves (or told to do so) from participation. The legislators’ public condemnation for my COVID treatment discussion failed to first disclose their conflicts of interests (nor allowed my

appeal/input). Their bullying process ignored protocol to insure scientific discussion. After the fact comments through the media were not vetted to meet scientific and ethical standards. For example, Sen Baker talks about my violation of a medical oath. Which one? Does she not realize that the “do no harm” principle has a more recent alternative (Prof Lasagna, 1964) in this era when we instead ask if benefits might outweigh risk of harm? If legislators’ invalid claims fall under the cover of their "free speech", then ironically they deny me mine, when in fact only physicians enter these areas of off-label treatment discussion. Specific rules that should have been followed were incorporated in versions of the international Helsinki Accord usually adopted by the US. For the latest version, the US refused to sign (because of a disagreement regarding placebo use in the control groups for HIV studies in Africa). When the US then cited their adherence to the rest of the Accord they were told to accept all or none. The US then resorted to the US Dept of Health and Human Services (DHHS) rules of the universally accepted Good Clinical Practice (GCP) to insure scientific principles of clinical experiments (including off label treatment studies). I have practiced, published and taught GCP principle for the World Health Organization from 1982-2005.

Incidentally, the oft quoted FDA message that one is promoting veterinary formulation of the off-label use of Ivermectin is but a strawman for my critics. Everyone in this field of GCP should know that veterinary formulations won't (and the reasons) meet Good Manufacturing Practices (GMP), a prerequisite even before GCP rules are approached. I summarized it for my students as follows: Why bother with the more sophisticated effort of valid human study design and analysis if the product (veterinary) itself is suspect and not consistent to begin with?

Agencies that I have Appealed to

I tried to pursue justice (for myself and other doctors who live in fear based on what has happened to me) through a few private law firms, the State AG's office, the federal Office of Special Counsel (OSC) and the Occupation Safety and Health Administration (OSHA), Hawaii Ethics Commission and the ACLU. I found many doors closed to me (or referral to other agencies) even before my full arguments were heard. The State's AG response is vague – they initially felt that what happened to me was only personal without rule violation, that my issues are very complicated for them and that they are busy with other cases such as bribery and corruption. As the IOM warned these latter types of monetary influences typically have been the focus of ethical reviews.

I have always contended that my defamation was indeed personal and for me a relatively minor aspect as I cleared my reputation (once my lawyer no longer restricted my speech) – but beyond personal issues are more important Federal whistleblower violations. In fact many false claims acts have no personal effects (enticements or threats) towards whistleblowers (termed the relator) but the violation is against the US government. The damage to society can be more subtle with much larger, later implications. In such cases the punitive fines are huge,

proportional to the status of the offender – so that violations are not repeated, simply, as the “cost of doing business”.

I pointed out that in the spirit of the oft cited Lincoln Law and false claims act (FCA) following the Civil War, there were no wrong “doors” to bring the cases of false claims forward. So far I have found no entry door to seek justice on this very important issue – ultimately affecting the future of medicine in the US. I personally have suffered neither significant retaliation nor kickbacks – and speak on behalf of the medical community which is now threatened by political bullies who violate rules with impunity (so far). Many feel that I have been “defamed” – but I have defended myself through my long career of accomplishments and public response to the allegations. More junior physicians do not have the confidence or experience to withstand bullying and may choose to remain quiet to not jeopardize their careers. Understandably, many may have second thought about entering the field of medicine.

2. My arguments

Many drugs (20-30%) used today in the US are in off-label status. I reference my detailed presentation on public televisions (Akaku) discussing the valuable role and caveats of off label drug use. It is a dangerous medical double standard to weaponize the rules especially when the bullies are themselves committing violations. How can the authorities criticize me for even discussing COVID off label use then quickly turn around and laud another off label drug for treatment of long COVID?.

<https://www.reuters.com/business/healthcare-pharmaceuticals/addiction-drug-shows-promise-lifting-long-covid-brain-fog-fatigue-2022-10-18>.

Open discussion without fear of political bullying is how medicine advances; not by silencing and demonizing the researchers and discussions. Worse are the ad hominin attacks for subject matter disagreements. For the sake of justice, so that judgments are not applied arbitrarily and capriciously, all doctors with off-label involvement should be threatened and defamed as I was. My colleagues have termed this the “scorched earth” principle. Tongue in cheek as this sounds, the alternative to apply justice unfairly can be even more devastating. This is exactly what prompted the previously mentioned “Crossroads” review. It is very telling that project directors offered to keep my three hour interview report anonymous for fear of retaliation. Obviously, I refused. I am guarded by the whistleblower protection rules – once the bullies recognize this framework of their own federal violations.

It is most ironic that the regulatory and legal community will not pursue, or help me pursue, violations on a topic where they cannot enter on subject matter alone (False claims Act for off-label medications). But there is a valid, quick fix to all of the above which I hope to present to

legislators who are willing to listen. I have already suggested this a few months ago to the consortium of universities conducting the “Crossroads” project. I hope that we can move forward past all of this ugliness – but there is recent evidence that we cannot – at least not yet in Hawaii.

Sometimes doctors can represent themselves without lawyers. But for Federal Whistleblower cases a lawyer is needed since the plaintiff really is the Federal government with everyone else acting on their behalf. Before I realized this I had planned to make my own arguments a follows:

Whereas (W) - The progress of medicine depends on medical research to understand the risk and benefit of new interventions, the research has to be done ethically and be scientifically sound. Some will say that bad science is a form of bad ethics, since patients volunteering to be “experimented on” (enrolled under guidelines of informed consent) understand that future patients may benefit. But this requires that study results are correctly interpreted, contributing to advancements in medical science. Otherwise, they put themselves at risk only for their own individual benefit.

W - In medicine and public health good science is founded on a few key principles time tested for the past several decades, that I practiced and taught for the past 40 years. One important rule, Good Clinical Practice (GCP) ,has been threatened by actions of the State legislature. Whether or not they fully understand the process/ principles of GCP they have instead chosen to attack the “messengers” as I tried to present these valuable GCP rules.

W - GCP: Scientists should welcome all questions and discuss the merit of each argument regardless of whose position it is.

They should feel free to switch positions and in the end the consensus cannot be attributed to any single participant. The scientific aspects of discussions cover: study design, data collection and analysis, conclusions drawn, publication of results and monitoring feedback to the publication. The State legislators attempted to block these federally mandated GCP practices through public personal attacks on physicians trying to discuss the value of GCP guidelines. They attack the product rather than the process which should be used to evaluate it. Furthermore, they confused the GCP arguments with Good Manufacturing Practices (GMP) when they refer to veterinary preparations of treatments instead of human formulations.

W - Another rule was violated by the State legislature. False Claims Act (FCA) permits only physicians to influence the use of off-label drugs. Off-label drugs are drugs that are approved for one use (with the safety profile known) to be given for another condition where the efficacy is yet to be determined. Typically, huge fines were levied against non-physicians promoting off-label drugs before they were approved. And now, conversely, those who blocked a drug in the off-label stages should be punished as well. The motive for this may be to promote a competing intervention. Without full disclosure of conflicts of interest we will never know, and is somewhat irrelevant to their actions.

W- While the legislature did not directly condemn GCP and off-label FCA rules, the actions of publicly shaming those who tried

to uphold them had a chilling effect on many medical scientists from further discussing/questioning the topic. Furthermore, I as a physician was not asked to defend my position prior to the public defamation by non-physicians for off-label drug use against COVID. After their public defamation my own attorney asked me to not respond publicly or to my accusers until the ruling by the medical board, several months later.

W- Once I was cleared by the Medical Board and not fired I finally got to present my science on the concepts and value of GCP (and yes, how it fully addresses veterinary formulators of drugs) both on Maui public TV and then published in Journal American Medical Association. I monitored both sites for feedback/comments and have nothing negative to date. When my position was made public some of my detractors seemed taken aback that I used arguments for off-label drugs. But then GCP rules apply to all drugs, yes (and I give references to my published work primaquine failure/malaria) even drugs after approval and marketing. They defended their initial attack that they did their “due diligence”. Am I now the cost of their “doing business as usual”?

W - Some will claim that the legislature acted during a crisis with passion and good intent. All who followed FCA and GCP rules were also acting with good intent. But we were following the law, and have been honored for practicing and teaching these rules for decades. These rules are in place especially for crisis situations. Beside claims of good intentions another

“reason” influencing one’s position could be conflict of interest. The medical field is so influenced by secondary motives that NEJM published first the false assurance that senior regulators could resolve this by self-control (NEJM, Steinbrook 2005). When this failed, NEJM again published new Institute of Medicine rules to show that conflict of interest goes beyond financial incentive to promotion of careers, positions and advancement. Furthermore, besides direct personal incentives, one must not act to favor friends, family, associates, colleagues and one’s students (NEJM, Steinbrook 2009). While the potential to be conflicted will be widespread, participation can continue but all must declare his/her conflicts to “clear the air”. To this COI I want to point out that the COVID pandemic has brought out a mirror image, conflict of fear – some will not be fully truthful, fearing that there will be repercussion by bullying authorities for alleged misinformation. We have made truth the first casualty of this crisis.

W - This is not an issue of free speech and neither I nor the legislators should try to use this argument. The American Civil Liberties Union (ACLU) cites another individual right besides free speech – that is the right to a fair trial/hearing before being punished. I contend that my initial punishment was public defamation – prior to which I was never asked to defend my position, though I have published and taught the topic for decades (including 6 publications on COVID).

W - For legislators who in hindsight want to admit to an error in judgement – they should apologize to the medical community, to lift this dark threat hanging over our heads. They committed bullying through allegations of misinformation, based on issues they are neither well versed in nor willing to be held accountable. For those who still think they are right – I am open to further discussion of this issue or they can submit their comments to JAMA for the editor to publish or not. And I will answer in JAMA if the editor passes them to me for comment.

W - There are many off-label drugs proposed for treating long COVID and other disease affecting residents of Hawaii. To only single out certain products, and then couple them to personal attacks is an example of applying rules/laws in a very arbitrary and capricious manner.

W - Besides the personal insults – calling doctors who support me “quacks”, based on the argument that we have violated our “oath” has to be addressed . I assume that the oath we violated is “to do no harm”. This is non-sensical when one is trying to balance risk versus benefit of new interventions. Surely anyone who practices/uses modern medicine realizes this paradox. In 1964 Prof Lasagna from Boston seemed to have resolved this issue, and some of his principles were incorporated by the IOM 50 years later.

W - with respect to medical practice and recommendations these subtle, ubiquitous conflicts of interest needs to be

controlled (NEJM R Steinbrook 2005 and 2009/IOM). We can have conflicts but they must be stated and judged against primary interests, valuable to society (patient/public interest, science, and education).

W - The violation of the False Claims ACT involved non-physicians influences to block off label medical interventions. Though my detractors did not falsely promote an off label drug their motive for blocking one will never be known. They tried to garner physician support for their defamation after the fact – but by then these physicians arguments can only enter a discussion mode with me. Alternatively, they could have responded to my JAMA publication with the editor passing comments to me for rebuttal, if he felt them valid – nothing was passed to me though many subsequent comments – mostly supportive were published.

W - it is hard to know the depth of my detractors knowledge of GCP and FCA rules since they did not engage in discussions with me before or after their public defamation. Perhaps they confuse GCP and GMP rules using the latter as “clear evidence” to imply violation of the former. I have also published GMP shortcomings (in Lancet 1984, for rabies vaccines).

W - My detractors did not focus on the product itself but on hearsay media “conclusions”, GMP and then personal attacks (that I was hiding behind credentials and violating my Oath).

W - everyone is entitled to free speech but beyond this, according to ACLU rules public, defamatory judgments by authorities based on alleged crimes also require a chance for the accused to defend themselves prior to the irreversible defamation. And now when will a public apology come after the fact?

W - Finally, in the heat of a crisis, errors will be made, but in hindsight failure to recognize (I am still open for discussion) or apologize for mistakes leaves many professional medical practitioners under threat of repeated abuses.

3. Reference Material

Senator Baker's public defamation:

<https://www.youtube.com/watch?v=PLteSp7pYCQ>

My scientific Akaku and JAMA responses: For the JAMA letter read the subsequent comments – none referred to me by JAMA editor for a response:

Below are the same AKAKU presentation via two sources.

Youtube Link: <https://youtu.be/IH3--W1zOMU>

Akaku.org Page: <https://www.akaku.org/government-on-demand/>

JAMA link with Dr Kim Pham:

<https://jamanetwork.com/journals/jama/fullarticle/2793357>

There was an additional comment by Sen Baker (Star Advertiser – which I have not listed as a reference). When I responded to her allegations in the media that I was referring to the area of Off-label treatment. She then said that she had done her due diligence and was not going “tit for tat” into further discussions. Also in

that article was a statement by a physician from UH who said that she herself would not recommend Ivermectin use for COVID. *This is an attempt to bring someone of physician status to counter my points of Off label use. It is now simply that, a discussion – prefaced by conflict of interest declarations...and opened to all physicians. Technically if this Hawaii doctor wanted to make her argument she should have addressed it to JAMA as a comment to my initial message. Many others did this and editor cleared many for add on-letters – nearly all were supportive. One slightly negative one JAMA published, but did not send it to me for my published “rebuttal”. There really was nothing worth rebutting so I left it to the editor of JAMA to facilitate this online “discussion”.*

Response from Clare Connors for not action at this time:

From PDF file 7 Nov 2023:

U.S. Department of Justice

United States Attorney

District of Hawaii

*PJKK Federal Building
300 Ala Moana Blvd., Room 6-100
Honolulu, Hawaii 96850*

November 7, 2023

(E08) 541-2850

F,4X(808) 54r-2958

VIA E-MAIL

Lorrin W. Pang, M.D., M.P.H.

Maui District Health Officer

Hawaii State Department of Health

panghl7l@gmail.com

Re: Conflicts of interest

Dear Dr. Pang:

*I write to acknowledge receipt of your letter regarding
potential conflicts of*

*interest and other alleged violations you reported while
you were the Medical*

*officer of Maui county. After review of your letter, we did
not identify a basis for*

our office to take federal action at this time. However, you may consider reaching

out to the United States Department of Health and Human Services, office of

Inspector General at <https://oig.hhs.eov/fraud/report-fraud/> to report your concerns.

Respectfully,

CLARE E. CONNORS

United States Attorney

District of Hawaii

DANAA. BARBATA

Assistant U.S. Attorney

4. Reference Federal Rules

Sometimes agencies asked me for specific rules which I claimed to be violated. These agencies usually, initially point out that the State legislature's attacks were only of a personal nature. When I do supply the following specifics there has been no response, other than a verbal comments during a joint call with the AG and Hawaii

Ethic Commission that the issue is complicated (for them) and not a high priority issue.

The references include 1) the Federal rules of Good Clinical Practice (GCP), with special point pertaining required evaluation of off-label studies. It is followed by 2) False Claims Act (FCA)

Good Clinical Practice The violation has to do with the long standing federal DHHS rule that clinical experiments must have their results for safety and effectiveness accurately analyzed and reported.

I cut and paste references and links to the latest Helsinki Accord rules and then the US GCP rules - both of which are being violated when Hawaii legislators threaten doctors (with me as an example) for even beginning to discuss the scientific aspects of clinical intervention studies:

Helsinki Version 2013 (most recent):

Preamble in: <https://www.wma.net/what-we-do/medical-ethics/declaration-of-helsinki/#:~:text=The%20first%20version%20was%20adopted,cited%20except%20for%20historical%20purposes.>

“...The Declaration of Helsinki (DoH) is the World Medical Association’s (WMA) best-known policy statement. The first version was adopted in 1964 and has been amended seven times since, most recently at the General Assembly in October 2013. The current (2013) version is the only official one; all previous versions have been replaced and should not be used or cited except for historical purposes. The WMA would like to thank all those who submitted comments and suggestions for the most recent revision of the DoH.”*

The preamble links to :

<https://www.wma.net/policies-post/wma-declaration-of-helsinki-ethical-principles-for-medical-research-involving-human-subjects/>

From the above:

“.....Research Registration and Publication and Dissemination of Results

35. Every research study involving human subjects must be registered in a publicly accessible database before recruitment of the first subject.

36. Researchers, authors, sponsors, editors and publishers all have ethical obligations with regard to the publication and dissemination of the results of research. Researchers have a duty to make publicly available the results of their research on human subjects and are accountable for the completeness and accuracy of their reports. All parties should adhere to accepted guidelines for ethical reporting. Negative and inconclusive as well as positive results must be published or otherwise made publicly available. Sources of funding, institutional affiliations and conflicts of interest must be declared in the publication. Reports of research not in accordance with the principles of this Declaration should not be accepted for publication.

Unproven Interventions in Clinical Practice

37. In the treatment of an individual patient, where proven interventions do not exist or other known interventions have been ineffective, the physician, after seeking expert advice, with informed consent from the patient or a legally authorised representative, may use an unproven intervention if in the physician's judgment it offers hope of saving life, re-establishing health or alleviating suffering. This intervention should subsequently be made the object of research, designed to evaluate its safety and efficacy. In all cases, new information must be recorded and, where appropriate, made publicly available. "

Having disavowed the latest Helsinki rules (due to a disagreement what treatment (placebo or US standard therapy) would be given to Africans in the control group of an HIV treatment study), the US did need to adopt the principles of doing good science for human research and they did so in the next attached reference outlining standard rules of Good Clinical Practice (GCP).

Incidentally, the oft quotes FDA message we support

using veterinary formulation for the off-label use of Ivermectin is but a strawman for my critics. It is basic to everyone in the GMP field why veterinary formulations won't pass the prerequisite Good Manufacturing Practices (GMP) to even progress to clinical trials under GCP. I have taught this principle for the WHO for decades and I summarized it for my students as follows: Why bother with the more sophisticated effort of human study design and analysis if the product itself is suspect and not consistent to begin with?

For GCP rules: See section on controversial 5th revision.

[https://en.wikipedia.org/wiki/Declaration_of_Helsinki#Fifth_revision_\(2000\)](https://en.wikipedia.org/wiki/Declaration_of_Helsinki#Fifth_revision_(2000))

The FDA adopted GCP rules instead of Helsinki after the 5th revision where the contentious point was comparator arm in HIV trials in Africa.

Here are relevant sections of the federal rules ICH E6(R2) Good Clinical Practice (GCP), updated versions occur often but the section numbering seems consistent for these important topics/principles.

1. Section 2.5 (Scientific Rigor):

- Emphasizes that clinical trials should be scientifically sound and ethically conducted.
- The goal is to ensure that outcomes are valid and credible, supporting the reliability of data for regulatory decisions.

2. Section 4.13 (Reporting and Dissemination):

- Mandates proper recording and dissemination of trial data.
- Ensures public and regulatory access to information to maintain transparency.

3. Section 5.18.2 & 5.18.3 (Addendum B - Monitoring Plans):

- Describes the requirement for risk-based monitoring approaches.
- Sponsors must focus on critical aspects affecting trial participant safety and data integrity.
- Addendum B stresses more adaptable and modern monitoring methods based on identified risks.

4. Section 6.7 (Protocol Amendments):

- Requires detailed documentation for any protocol amendments.
- Ensures that changes do not undermine the scientific integrity or participant safety.

5. Section 6.8 (Trial Closure):

- Focuses on documentation and reporting once a trial concludes.
- Emphasizes the need to analyze trial data, secure findings, and close out properly with regulatory bodies.

If you need further information or more specific details on any of these, you can access the FDA's Clinical Trials Guidance section.

My detractors are welcome to argue further whether my science is sound but they should show that they have read all my background material (including my own cited publications), declare their conflicts of interest IAW IOM policies, review the grounds on which the Hawaii State Board of Medical Examiners cleared me (reasons redacted/opaque to me), show publication of their arguments (as I have done in JAMA). Scientific discussion

can be either public or private and retaliation based on disagreements is forbidden.

2. False Claims Act

Federal Food, Drug, and Cosmetic Act (FDCA):

- Under the FDCA, drug manufacturers must obtain FDA approval for the specific indications (uses) of their drugs. Promoting or marketing a drug for any off-label use without FDA approval is considered **misbranding**, which is illegal.
- Section 502(f) of the FDCA outlines that labeling (including marketing and promotion) must include adequate directions for the drug's approved uses. Promoting off-label uses violates this requirement because those uses have not been evaluated and approved by the FDA.

2. False Claims Act (FCA):

- Companies that promote off-label uses can also be prosecuted under the **False Claims Act**. If a pharmaceutical company promotes a drug off-label and, as a result, false claims are submitted to government healthcare programs (such as Medicare or Medicaid) for reimbursement of that off-label use, the company can be fined for defrauding the government.
- **Whistleblower lawsuits** under the False Claims Act have led to significant penalties for pharmaceutical companies engaging in off-label promotion.

3. Anti-Kickback Statute:

- In some cases, companies may attempt to incentivize physicians or other healthcare professionals to promote or prescribe drugs for off-label uses. This practice could violate the **Anti-Kickback Statute**, which prohibits providing financial incentives to encourage the use of drugs covered by federal healthcare programs.

Legal Penalties:

Pharmaceutical companies that are found to be promoting off-label uses can face substantial fines and

legal penalties. Some of the largest fines in history have been imposed under these laws. Examples include:

- In 2009, Pfizer paid a **\$2.3 billion settlement** for illegally promoting the painkiller Bextra for off-label uses.
- In 2012, GlaxoSmithKline (GSK) paid **\$3 billion** in a settlement involving the off-label promotion of several drugs, including the antidepressant Paxil.

In summary, it's the **FDCA** (under the authority of the FDA) and other related statutes like the **False Claims Act** and the **Anti-Kickback Statute** that prohibit pharmaceutical companies from promoting drugs for off-label uses, and violations of these laws result in significant penalties.

Here is the Chatgpt response to my query about the mirror image of non-physicians blocking off-label drugs.

False claims act has been applied to drugs under off label status being promoted. Are there mirror image issues with non-physicians blocking competing off-label drugs in lieu of other experimental drugs.

ChatGPT said:

ChatGPT

The False Claims Act (FCA) has been a significant tool in regulating the pharmaceutical industry, particularly in cases involving off-label drug promotion. When pharmaceutical companies promote drugs for off-label uses—uses not specifically approved by the FDA—they may be violating the FCA if those promotions lead to fraudulent billing to federal healthcare programs, like Medicare or Medicaid. The law allows individuals (whistleblowers) to sue on behalf of the government, often leading to substantial financial penalties for companies found in violation.

Mirror Image Issues

1. Blocking Competing Off-Label Drugs:

- **Non-Physician Interference:** Non-physicians, such as pharmacists or administrative staff, may play a role in the approval or dispensing of medications. If these individuals block access to certain off-label drugs in favor of other experimental drugs, it raises ethical and legal questions.
- **Competition and Innovation:** This interference could stifle competition and innovation, particularly if the off-label drugs have proven

efficacy for specific conditions. (now we will never know because threats have stifled GCP for Ivermectin, specific to each COVID variant) - see my Akaku comments to NEJM Brazil study and then JAMA). Patients may be denied effective treatment options based on decisions made by non-physicians, which could lead to health risks and poorer outcomes.

2. Regulatory and Legal Considerations:

- **Off-Label Use Legality:** Physicians can prescribe medications off-label, but the promotion of these uses by drug manufacturers is tightly regulated. If non-physicians are influencing these prescribing decisions based on non-evidence-based criteria, it could be seen as a violation of patient rights and medical ethics.
- **False Claims Implications:** If off-label drugs are being blocked and patients are pushed towards experimental drugs (and vaccines) without adequate evidence of their effectiveness, it may create grounds for False Claims Act suits if these actions lead to fraudulent billing or harm to patients.

3. Patient Autonomy and Informed Consent:

- * key paragraph, exactly what State Legislators did: Patients should have the right to access information about all available treatment options, including off-label drugs. If non-physicians are making decisions that limit this access, it raises issues of informed consent and patient autonomy.

4. Incentives and Financial Conflicts:

- Non-physicians may have incentives (financial or otherwise) to promote certain drugs over others. This could lead to ethical dilemmas and conflicts of interest, especially if they are benefiting from the sale of the experimental drugs (and vaccines).

Conclusion

There are indeed mirror image issues in the context of non-physicians blocking access to off-label drugs while promoting experimental ones. These issues intertwine with legal, ethical, and regulatory frameworks governing drug promotion and patient care. Addressing these challenges may require stricter guidelines and oversight

to ensure patient safety and fair access to treatment options.

4o mini

Here is a list of the larger FCA awards over a 20 year span:

https://en.wikipedia.org/wiki/List_of_largest_pharmaceutical_settlement

The following is a big list of the 20 largest settlements reached between the United States Department of Justice and pharmaceutical companies from 1991 to 2012, ordered by the size of the total settlement. The settlement amount includes both the civil (False Claims Act) settlement and criminal fine. Glaxo's \$3 billion settlement included the largest civil False Claims Act settlement on record,[1] and Pfizer's \$2.3 billion (\$3.5 billion in 2022) settlement including a record-breaking \$1.3 billion criminal fine.[2] Legal claims against the pharmaceutical industry have varied widely over the past

two decades, including Medicare and Medicaid fraud, off-label promotion, and inadequate manufacturing practices.[3][4] With respect to off-label promotion, specifically, a federal court recognized off-label promotion as a violation of the False Claims Act for the first time in *Franklin v. Parke-Davis*, leading to a \$430 million settlement.[5]

Year ↕	Company ↕	Settlement ↕	Violation(s)	Product(s) ↕	Laws violated (if applicable) ↕
2012	GlaxoSmithKline^{[1][6]}	\$3 billion (\$1B criminal, \$2B civil)	Criminal: Off-label promotion, failure to disclose safety data. Civil: paying kickbacks to physicians, making false and misleading statements concerning the safety of Avandia, reporting false best prices and underpaying rebates owed under the Medicaid Drug Rebate Program	Avandia (not providing safety data), Wellbutrin , Paxil (promotion of paediatric use), Advair , Lamictal , Zofran , Imitrex , Lotronex , Flovent , Valtrex	False Claims Act , FDCA
2009	Pfizer^[2]	\$2.3 billion	Off-label promotion, kickbacks	Bextra , Geodon , Zyvox , Lyrica	False Claims Act , FDCA
2013	Johnson & Johnson^[7]	\$2.2 billion	Off-label promotion, kickbacks	Risperdal , Invega , Nesiritide	False Claims Act , FDCA
2012	Abbott Laboratories^[8]	\$1.5 billion	Off-label promotion	Depakote	False Claims Act , FDCA
2009	Eli Lilly^[9]	\$1.4 billion	Off-label promotion	Zyprexa	False Claims Act , FDCA
2001	TAP Pharmaceutical Products^[10]	\$875 million	Medicare fraud , kickbacks	Lupron	False Claims Act , Prescription Drug Marketing Act
2012	Amgen^[11]	\$762 million	Off-label promotion, kickbacks	Aranesp	False Claims Act , FDCA
2010	GlaxoSmithKline^[12]	\$750 million	Poor manufacturing practices	Kytril , Bactroban , Paxil CR , Avandamet	False Claims Act , FDCA
2005	Serono^[13]	\$704 million	Off-label promotion, kickbacks , monopolistic practices	Serostim	False Claims Act
2008	Merck^[14]	\$650 million	Medicare fraud , kickbacks	Zocor , Vioxx , Pepsid	False Claims Act , Medicaid Rebate Statute
2007	Purdue Pharma^[15]	\$601 million	Off-label promotion	Oxycontin	False Claims Act
2010	Allergan^[16]	\$600 million	Off-label promotion	Botox	False Claims Act , FDCA
2010	AstraZeneca^[17]	\$520 million	Off-label promotion, kickbacks	Seroquel	False Claims Act
2007	Bristol-Myers Squibb^[18]	\$515 million	Off-label promotion, kickbacks , Medicare fraud	Abilify , Serzone	False Claims Act , FDCA

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2010	Allergan ^[16]	\$600 million	Off-label promotion	Botox	False Claims Act, FDCA
2010	AstraZeneca ^[17]	\$520 million	Off-label promotion, kickbacks	Seroquel	False Claims Act
2007	Bristol-Myers Squibb ^[18]	\$515 million	Off-label promotion, kickbacks, Medicare fraud	Abilify, Serzone	False Claims Act, FDCA
2002	Schering-Plough ^[19]	\$500 million	Poor manufacturing practices	Claritin	FDA Current Good Manufacturing Practices
2006	Mylan ^[20]	\$465 million	Misclassification under the Medicaid Drug Rebate Program	EpiPen (epinephrine)	False Claims Act
2006	Schering-Plough ^[21]	\$435 million	Off-label promotion, kickbacks, Medicare fraud	Temodar, Intron A, K-Dur, Claritin RediTabs	False Claims Act, FDCA
2004 ^[22]	Pfizer	\$430 million	Off-label promotion	Neurontin	False Claims Act, FDCA
2008	Cephalon ^[23]	\$425 million	Off-label promotion ^[23]	Actiq, Gabitril, Provigil	False Claims Act, FDCA
2010	Novartis ^[24]	\$423 million	Off-label promotion, kickbacks	Trileptal	False Claims Act, FDCA
2003	AstraZeneca ^[25]	\$355 million	Medicare fraud	Zoladex	Prescription Drug Marketing Act
2004	Schering-Plough ^[26]	\$345 million	Medicare fraud, kickbacks	Claritin	False Claims Act, Anti-Kickback Statute