Minneapolis’s Hennepin County Medical Center finds itself in hot water [2] over allegedly systemic practices that, in concert, might have violated individual human rights and, as a result, have prompted a formal U.S. Food and Drug Administration (FDA) review. Central to the investigation is whether the institution spanning from leadership to oversight boards adhered to strict, narrow regulatory exemption standards in their high-risk clinical trials that allow for inclusion of a patient without his or her knowledge or consent.

Wrought with bioethical concern to begin with, this often little-known to the public and even many health professionals limited waiver of consent was designed to have rare use in emergency medicine research. And meet very strict measures due to the gravity of its nature in the first place.

What happened
A healthcare watchdog group believed the actions of the health system were so egregious that in July they sent a comprehensive letter to the FDA and the Office for Human Research Protections (OHRP). In it, they requested investigation into Hennepin’s other clinical trials and their oversight and executive membership bodies, imposing severe sanctions and basically maintained the ketamine trials performed by the facility did not meet the consent exception requirements, lacked safeguard protections for the extremely vulnerable population it studied (eg seeking consent from family when impaired), exceeded the minimal risk standard subjecting individuals to meaningful harm and did not satisfy fundamental ethical principles. They further implied the off-label use of the drug for pre-hospital agitation in their studies was a way to circumvent often burdensome governmental regulations of new drugs.

The FDA took action, investigated in August, and released their findings to which the consumer advocacy organization published a second letter including them (see here) with more forceful language and recommendations. As reported in STAT News, for example, “The FDA inspectors found that “some or all of the subjects [in four studies] were likely to be vulnerable to coercion or undue influence.” The ramifications will be interesting to watch play out.

But, let’s delve into the prominent regulatory issues

Are you aware that when it comes to emergency medical research there is a restricted set of circumstances where not getting informed consent is permissible? Did you know if you or a loved one sustained a cardiac arrest the decision to give you a potentially life-saving heart medication or placebo, in the fleeting moment where seconds matter, might be made at random by those coordinating a study? That you likely have no say due to regulations that could exempt the sponsor of such work from getting informed consent if it isn’t “feasible” to obtain?

The cardiac arrest example took place in a recent National Institutes of Health (NIH) sponsored study detailed here. A constituent alerted Congress of his dismay when his anguish over the loss of his wife was compounded by discovering after her death that she was automatically enrolled and he had never been given an opportunity to object.

Intended to make headway in conditions where not much scientific progress and medical advance has taken place and superior options for treatment are unsatisfactory, the U.S. Food and Drug Administration (FDA) set forth guidelines that detail very specific circumstances where exemption from informed consent research is permitted (see guidelines here). The interventions being investigated should not fall below the accepted standard of care to endanger the patient. Additionally, the research must be publicized to the communities in which it is conducted to alert citizens of their ability to opt out and participating personnel (in these cases, EMS workers) must be properly trained to get informed consent when or if feasible - strict adherence is required.

But, is “if feasible” more a theoretical than practical consideration in a situation like cardiac arrest? And, in the case of Hennepin it appears efforts to safeguard the protections of the particularly vulnerable population it studied fell demonstrably short.

I would argue truly informed consent (in the cardiac arrest arrest example in particular) under these circumstances is implausible. First it is a substantial diversion away from patient care under life-threatening conditions, possibly adversely impacting survival. Second, it shifts the burden of
consequences of that decision to a family member, if even present or reachable, who may be unprepared to make such a split-moment choice.

The Medical Ethics

The Hennepin scenario is deeply troubling. Those who received ketamine by paramedics instead of the alternative had a significant risk of serious complications. Additionally, due to the flaws in study approval and design, some patients who might not have required any medicine at all for pre-hospital agitation, if standard of care were instead enacted, were unnecessarily put at risk.

While Hennepin’s fate is unclear in terms of repercussions, the NIH cardiac arrest scenario additionally raises concern over the viability of this exception policy - regardless of how precisely and accurately it is interpreted. To genuinely appreciate the ethical considerations, please read Did NIH Play Ethical Roulette? [5]

If the FDA guidelines [6] on exception for informed consent in emergency medicine research are interpreted sub-optimally albeit by misstep or more nefarious intent, a patient's ignorance of participation in a clinical trial erodes his or her autonomy whether the participation is in an emergency setting or not. Investigation and understanding the alleged system breakdowns is extremely important, because they appear to be occurring in other situations than mentioned here.

A public conversation about the suitability of the current guidelines appears to be way overdue and worthwhile. If universal understanding of this exemption remains under the radar, then instances like these will cause irreparable damage to public trust in institutions and undermine the health care they seek.

My recent article over the ethical considerations of Would Automatic Organ Donor Status Fly in the United States? [7] seems less hypothetical today.