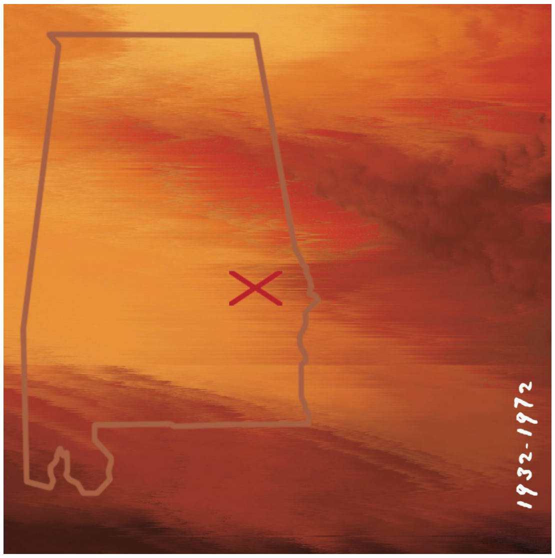
MISCONDUCT IN RESEARCH:

ROOM TO IMPROVE

The history of clinical research is often studied as an important foundation for understanding the principles that guide modern human subjects research.

The abuses of the past spurred the creation of the Nuremburg Code and the Declaration of Helsinki; the Belmont Report, ICH Good Clinical Practice and ISO 14155 guidelines (among others) have further expanded our understanding of the requirements for ethical and sound studies. The risk of only studying historical abuses like Nazi experimentation or the Tuskegee Syphilis study is that they seem like distant, shameful reminders of human cruelty, when in reality abuses, fraud, and misconduct are unfortunately still happening in research today. These foundational principles for ethical research are still relevant and essential; however, the study of clinical research is not complete without researching the history behind these values and their modern relevance.

Two well-known recent examples include the death of Jesse Gelsinger in 1999 from his enrollment in a gene therapy study (despite not meeting the entry criteria) where the investigator had a significant financial conflict of interest (Wilson, 2010). Secondly, in the Ketek Trial, where the highest enrolling investigator enrolled many ineligible or nonexistent patients, going so far as to forge consent documents and falsify data (Dunn, 2012). These examples alone may provide enough evidence of ongoing abuses in research, but unfortunately, there are additional examples.



WARNING

Further evidence of continuing problems in clinical research becomes clear after reviewing warning letters issued (and publicly available online) by the FDA. Year after year, sponsors, IRBs and investigators are cited for inadequate oversight, deviating from the clinical trial protocol, improper informed consent procedures, among other issues. Over the past two decades, the number of warning letters issued shows an increasing trend (Talele, 2012). While errors are inevitable in the complex world of clinical research, the citations within warning letters are serious because they may have immediate or future effects on human subject safety.

Thankfully, research abuses at the level of the familiar historical examples do not seem to occur in modern research to such an extreme degree. Some may claim that this is reason enough to state "research abuse is a thing of the past," but only if abuse is taken in the most extreme interpretation possible. Gupta (2013) reported that approximately 23% of FDA inspections are considered for-cause. The pressure to publish important results, gain the respect of peers, and obtain financial benefits can all contribute to the reasons why misconduct still occurs today. According to Bhatt (2011), poor quality in research like protocol deviations, inadequate records, and failure to secure compliance erode the public trust in clinical trials and undermine their positive influence on the future.

In another example of contemporary clinical trial misconduct, a researcher named Anil Potti published falsified data in 2006, which supported three clinical research trials at Duke University for personalized cancer treatments (Gewin, 2012). Due to the persistence of biostatisticians Keith Baggerly and Kevin Coombes over four years, the data was shown to have been manipulated. Further, it was discovered that Potti had provided false claims on his CV, including that he was a Rhodes Scholar. As a result, ten papers authored by Potti were retracted and the trials were eventually stopped in November 2010.

In 2013, the NIH-funded SUPPORT study was accused of not properly disclosing the risks to premature babies in a study on oxygen levels in the informed consent forms used by several research institutions. The levels of oxygen were described as within the standard of care; however there was evidence before the trial that certain oxygen levels could influence infant mortality and blindness (Tavernise, 2013). Further, the NIH has been accused by a research ethics watchdog group of interfering with an independent review of the circumstances by the OHRP; the group is now calling for an investigation by the Department of Health and Human Services.

The issues cited in warning letters may not always seem like obvious human rights abuses, but the combination of these with examples like Jesse Gelsinger's death, the Ketek trial, Anil Potti's falsified data, and the NIH's informed consent errors creates a picture of clinical research that still has a long way to go to meet the principles established decades ago for ethical clinical research.

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Rachel joined IMARC in 2011 as a Clinical Research Associate after previously working in the medical device research and development field. Utilizing her background as an engineer, Rachel brings a unique perspective and valuable tool set to the IMARC team. Her critical thinking skills allow her to apply the regulations across various protocols and have influenced her advancement to her current position of Clinical Auditor.

Rachel assisted IMARC in achieving ISO 9001 certification with the implementation of a robust quality management system in August 2014. She has been a member of the Association of Clinical Research Professionals since 2011 and became a Certified Clinical Research Associate in 2013. She holds a Bachelor of Science degree in Biomedical Engineering from Case Western Reserve University and is currently enrolled in the Clinical Research Administration Master's program through The George Washington University.

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