**Table 2: A few prominent examples of ethically unjustified trials disobeying the Code**

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| Year | Case | Details | Consequences |
| 1966 | **Beechers’s Article**: Henry Beecher, pioneering American anaesthesiologist and medical ethicist, published a landmark article quoting 22 examples of ethically questionable clinical studies. | One of his examples was **the assessment of severity of streptococcal pharyngitis without the treatment of sulphadiazine**. Although, it was known that Penicillin can be given to avoid rheumatic fever, it was denied to a group of 500 uninformed patients to observe the severity of rheumatic fever. The subjects also included a control group and an exudative group ‘A’ streptococcus. The latter received only non-specific treatment i.e. no Sulphadiazine. 5.4% of those treated with Sulphadiazine and 4.2% in the control group were diagnosed with rheumatic fever. (12) | “The subjects were not informed, did not consent and were not aware that they had been involved in an experiment”, was the written statement of a medical officer of that case.  This revolutionary article proved to be a significant tool in making informed consent mandatory for any experimentation involving human subjects. (13) |
| 1932- 1972 | **Tuskegee Syphilis Study**: The U.S. Public Health Service (USPHS) initiated a study, in 1932, to study the natural progression of untreated, latent syphilis in black males. It was conducted in Tuskegee, Alabama. The study involved the selection of black syphilitic males of the age twenty-five to sixty. (14) | The study included 600 African- American men comprising of 400 syphilitic men whereas, 200 uninfected men as the control group. Meanwhile, in 1930s heavy metal treatment and in 1950s Penicillin became abundantly available for the treatment for syphilis, but the men were denied both the therapies to let the disease progress further. (15)  The study was originally intended to be carried out for about six months but practically continued for over 40 years which is undoubtedly a celestial difference. | In 1972, the details of the study were released publically by the national press. By the time, the study was finally ceased, the casualties from advanced syphilitic lesions had exceeded 100. In 1972, the study was declared to be ethically unjust and argued that the subjects should have been treated with Penicillin.  A special commission was appointed, ‘The National Commission for Protection of Human Subjects of Biomedical and Behavioural Research’. (16) The report submitted by this commission, ‘**The Belmont Report’,** aimed at compiling a set general philosophical principles to govern the medical ethics. |
| Mid 1950s- 1970s | **Willowbrook school case:** Children were infected with live hepatitis virus by the Dr Saul Krugman and his team of investigators to study the scope for development of a hepatitis vaccine in Willowbrook State School, an institution for intellectually disabled children on Staten Island, New York. (17) | The researchers were adamant that they were simply engaging observational studies. However, the truth be said, they were exploiting a socially vulnerable population under the impression of scientific progress. (18) |  |
| 1951 | **Henrietta Lacks case**: Henrietta Lacks, a young woman and mother to five kids, visited The Johns Hopkins Hospital reporting vaginal bleeding. Dr Howard Jones, post the examination, found a large, malignant tumour on her cervix.  (19) | Dr Gey, a prominent cancer and virus researcher, had been collecting cell samples from all the cervical cancer patients at The Johns Hopkins Hospital. Unfortunately, none of the sample cells survived for a prominent duration except Mrs Lacks’ cells which divided approximately two folds each day. | The cells, named as ‘HeLa’ cells, are used to study the effects of various drugs, hormones and viruses on the growth of cancer cells without experimenting on humans. They have been used to study the human genome and played a huge role in the development of the polio vaccine (19), (6) |
| 1994 | The AZT trials in African and other developing countries: The ACGT (AIDS Clinical Trial Group) reported that administration of AZT (Zidovudine) in pregnancy, during labour and in neonates reduces the chances of MTCT (Mother to child transmission) by approximately 66.6%. | As the regimen of AZT was not affordable to the HIV positive mothers in Africa, where the incidence of HIV was high, the World Health Organization decided to find an economical way around it.  Many placebo controlled trials were conducted in Asia and Africa as they would not have been accepted in developed countries which clearly highlights its double standard nature. | In this case, many neonates could have been saved which were otherwise not as their mothers received placebos and not the drug.  (20) |
| 1966 | **The ‘Trovan’ (Pfizer) study case** **in Nigeria:** Kano State, in 1966, witnessed an epidemic of cerebro-spinal meningitis majorly affecting the children. | Pfizer organized a study, where it enrolled around 200 children categorizing them into two sections- one receiving the test drug ‘Trovafloxacin’ (Trovan), which is a quinolone antibiotic (oral) and the other as the control section receiving Ceftriaxone or Chloramphenicol. The subjects were recruited within 3 weeks of commencing the study.  The study was heavily criticised for disobeying the fundamental ethical laws. **The allegations were as follows:**  1. An ethical clearance was not obtained prior to the study.  2. No informed consent was obtained from the participants. Neither the participants were provided with any prior knowledge about the purpose or process of the research being conducted.  3. Vulnerable population of poor, illiterate people was capitalized on the grounds of research.  4. The company did not bother to take care of the ongoing epidemic once the study was over. | The experiment was declared as an illegal trial of an unregistered drug due to absence of any ethical clearance. Consequently, Pfizer agreed to a $75 million out of court settlement. (20) |