PAPER N. 13

When the researcher becomes the subject: the dangers of unregulated self-experimentation

BEATRICE GEUSA

Trento BioLaw Selected Student Papers

Jean Monnet EUROPEAN CENTRE UNIVERSITY OF TRENTO

Co-funded by the Erasmus+ Programme of the European Union

UNIVERSITÀ DEGLI STUDI DI TRENTO
Facoltà di Giurisprudenza

I paper sono stati selezionati a conclusione del corso *BioLaw: Teaching European Law and Life Sciences (BioTell)* a.a. 2018-2019, organizzato all'interno del Modulo Jean Monnet "BioLaw: Teaching European Law and Life Sciences (BioTell)", coordinato presso l'Università di Trento dai docenti Carlo Casonato e Simone Penasa.

When the researcher becomes the subject:

the dangers of unregulated self-experimentation

Beatrice Geusa[*]

ABSTRACT: The aim of this paper is to present an overview on self-experimentation and the scarce legal framework related to it. This is done by analyzing human experimentation and its regulation, and how it could be applied to self-experimentation. Additionally, the practice is compared to the introduction and the functioning of Right to Try laws. Lastly, the lack of legislation on self-experimentation is addressed, providing an explanation on why an ethical and legal framework of reference is needed.

KEY-WORDS: Self-experimentation; Human experimentation; Nuremberg Code; Declaration of Helsinki; Right to try

1. Introduction

Self-experimentation is an ever-present practice that has evolved throughout history, along with the wider field of human experimentation in which it is comprised. However, as regulations were enacted and evolved in regard to human experimentation in general, leading to the well regulated procedures and protocols that are provided today for clinical trials, self-experimentation remains close to totally unregulated.

As a phenomenon that is rapidly changing and spreading, especially in recent times, the complete lack of a legal framework appears odd, and begs the question: is the increase in self-experiments "just a phase" or is this reckless and possibly highly risky practice unduly overlooked by legislators?

[*] *Studentessa dell'Università di Trento, Facoltà di Giurisprudenza.*

2. Human experimentation

Human experimentation can be defined as «anything done to an individual to learn how it will affect him». Its main purpose is to obtain new scientific knowledge rather than the development of therapies itself[1], which means that even if an experiment is ultimately beneficial to other patients, or even to the subject himself, it does not necessarily serve an important purpose for medicine in general[2]. On the contrary, an experiment that has negative effects on the patient can result in new scientific discoveries, or may help the research move forward, and might therefore be considered meaningful.

In general, the treatment of human subjects can be roughly divided in three main areas. The first area is that of traditional treatment, consisting in normal and approved methods and techniques used on patients for therapeutic purposes. The second one is defined as research treatment, better known as therapeutic experimentation, which entails new methods and techniques tested on the patient for therapeutic purposes as well. The third encompasses research experimentation, as in research concerning new procedures and drugs, tested purely for scientific purposes[3]. If the entirety of medical progress was to depend exclusively upon the potential side-effects of traditional treatments or incidental scientific byproduct of therapeutic experimentation, medical science and human health care might not have undergone the breakthroughs and discoveries that shaped it into what it is today[4]. In this development process, human experimentation was the central mean to perform both therapeutic and research experimentation.

As a multifaceted phenomenon, it has presented itself in different guises throughout history, at times even in the shape of “inhumane” experimentation. In light of this, there have been many attempts to discipline the practice over the years, not all of them effective. The Nuremberg Medical Trials, and the international conventions that followed them, can be regarded as the turning point in the field at stake.

3. An overview of International regulations

[1] M. Cheriff Bassiouni, T.G. Baffes, J.T. Evrard, *An appraisal of human Experimentation in International Law and Practice: The need for international regulation of human experimentation*, in *The journal of Criminal Law and Criminology Northwestern University School of Law,* 1981, 1597.

[2] W.F. Bowker, *Experimentation on Humans and Gifts of Tissue: Articles 20-23 of the Civil Code,* in *McGill Law Journal*, vol.19, 1973, 161 – 164.

[3] D. Giesen, *Civil Liability of Physicians for New Methods of Treatment and Experimentation: A Comparative Examination*, in *Medical Law Review*, Vol.3, Issue 1, 1995, 22-25.

[4] M. Cheriff Bassiouni, T.G. Baffes, J.T. Evrard, *op. cit.,* 1597.

The first example of international regulation is the Nuremberg Code, developed by US judges soon after the Nuremberg Medical Trials that followed WWII. During the war, Nazis experimented on concentration camp prisoners, performing horrific non-therapeutic and non-consensual research[5] (see *infra*). The Nuremberg Code, despite its inherent limitations due to its origins, remains the most authoritative legal and ethical document governing the research field, setting standards at an international level. It is also considered one of the main documents of reference in the human rights landscape[6].

The legal framework set by the Code is focused on voluntary, informed, competent and comprehensive consent and the consequential right to withdraw from a pending experiment. The set of provisions listed in it regulate different aspects of the practice: from the subjects to the purpose of the experiments, the condition under which they must be performed and the individuals qualified to conduct them. The basic principles enumerated include: the avoidance of unnecessary physical and mental suffering and injury; the absence of any *a priori* reason to believe that death or disabling injury will occur as a result of the experiment; the need for an evaluation of the risks, that must never exceed the benefits; and the presence of a qualified researcher prepared to terminate the experiment if it becomes «likely to result in the injury, disability, or death of the experimental subject»[7].

The Declaration of Helsinki was the second formal attempt to place human experimentation within the boundaries of a framework[8], this time designed by physician-researchers instead of jurists.

In fact, many medical practitioners felt that the Code, being devised by judges during a trial, was not compatible with the reality of medical research. The Declaration, on the other hand, is essentially a guide «from physicians to other physicians»[9]. As such, the result was more permissive and paternalistic than the previous document: it is an ethical, as opposed to legal, set of guidelines[10]. Nonetheless, several jurists such as Jochen Taupitz claim that even «though [the Declaration] is not a legally binding instrument under international law, [its] influence on medical ethics and national regulations on biomedical research cannot be overstated»[11]. Just as the Nuremberg Code, the above-mentioned Declaration revolves around the protection and respect of individuals, «whilst emphasizing their right to self-determination and the right to

[5] G.J. ANNAS, *The Changin Landscape of Human Experimentation: Nuremberg, Helsinki and Beyond,* in *Health Matrix: The Journal of Law-Medicine,* Vol.2, Issue 2, 1992, 119 Available at: http://scholarlycommons.law.case.edu/healthmatrix/vol2/iss2/3 (last consulted on 08/11/2018).

[6] G.J. ANNAS, *op. cit.,* 121.

[7] The Nuremberg Code, available at: https://history.nih.gov/research/downloads/nuremberg.pdf (last consulted on 08/11/2018).

[8] L.E. BRYANT JR., *The Burgeoning Law of Medical Experimentation Involving Human Subjects*, in *The John Marshall Law Review*, Vol. 8, 1974, 19-20.

[9] G.J. ANNAS, *op. cit.,* 122.

[10] W. REFSHAUGE, *The Place for International Standards in Conducting Research for Humans*, in *Bullettin of the World Health Organization,* Vol.55, 1977, 133-135.

[11] E. DEUTSCH, J. TAUPITZ, *Freedom of control and biomedical research*, in *Bulletin of Medical Ethics,* 1999.

make informed decisions (Articles 20, 21 and 22) concerning participation in research, both initially and during the course of the research»[12]. Additionally, the Declaration enumerates a set of operational principles to better regulate the research process (see *infra*).

In 1975 physicians developed a new set of guidelines, identified as Helsinki II, that was conceived to supersede Helsinki, although it was also aimed at superseding the Nuremberg Code as well[13]. Nevertheless, such an intent was deemed impossible by jurists, as the Nuremberg Code is considered to be the basis for international law and ethics in the area of human experimentation. Thus, lowering its standards can be done neither by a group of researchers, nor by the legal rule of an individual country: states can only add provisions and raise the standards that are already envisioned by the Code[14].

The third example is the Declaration of Geneva (also known as Physician's Pledge), adopted by the General Assembly of the World Medical Association (WMA) in 1948. This document was aimed to physicians and it was intended as a revision of the Hippocratic Oath, in light of WWII events[15]. The WMA wanted to create a set of guidelines regarding both human rights in general and the rights of patients, reforming the area of medical ethics. It was drafted in the form of an oath, that even nowadays still has to be taken by physicians all around the world to ensure the safety of patients.

The pledge contains a set of principle to be followed, such as: respect of the autonomy and dignity of the patient; respect for human life; non-discrimination of the patients; use of medical knowledge only for the benefit of the patient, and the advancement of healthcare and not to violate human rights and civil liberties, even under threat[16].

The fourth main international document in the human rights field is the Convention for the Protection of Human Rights and Dignity of the Human Being with regard to the Application of Biology and Medicine: the Convention on Human Rights and Biomedicine, also known as Oviedo Convention, signed in 1997.

[12] Declaration of Helsinki, available at: https://www.wma.net/policies-post/wma-declaration-of-helsinki-ethical-principles-for-medical-research-involving-human-subjects/ (last consulted 08/11/2018).

[13] 1982 CIOMS Guidelines available at: https://cioms.ch/wp-content/uploads/2016/08/International_Ethical_Guidelines_for_Biomedical_Research_Involving_Human_Subjects.pdf (last consulted 08/11/2018).

[14] G.J. ANNAS, *op. cit.,* 124.

[15] Declaration of Geneva, available at: https://www.wma.net/policies-post/wma-declaration-of-geneva/ or https://en.wikipedia.org/wiki/Declaration_of_Geneva (last consulted 08/11/2018).

[16] Declaration of Geneva, available at: https://www.wma.net/policies-post/wma-declaration-of-geneva/ (last consulted 08/11/2018).

This Convention is the only international legally binding instrument on the protection of human rights in the biomedical field, and it is mainly based on the European Convention on Human Rights[17]. It can be qualified as a framework Convention aiming at «protecting dignity and identity of all human beings and guaranteeing everyone, without discrimination, respect for their integrity and other rights and fundamental freedoms with regard to the application of biology and medicine» (Article 1)[18]. The fundamental principles enumerated in the Convention are to be applied to daily medical practice, including biomedical research, genetics and transplantation of organs and tissues, and the document is regarded as an «European treaty on patient's rights»[19]. The core around which revolves the entire Convention is the need for free, informed, express, specific, and documented consent of the person involved in the research.

These requirements are differentiated and tailored to the needs of each field disciplined by the Convention and its additional protocols. Specifically, the additional protocol concerning Biomedical research is intended to adapt the standard principles embodied in the Convention, especially the aim to protect human rights and dignity, in this specific field: i.e. the principle of consent is to be referred to the person(s) participating in biomedical research.

Moreover, the Protocol addresses issues such as: risks and benefits of research; protection of persons not able to consent to research; scientific quality; independent examination of research by an ethics committee; confidentiality and the right to information; undue influence; safety and duty of care[20].

The last document to be analyzed in the framework of human experimentation regulations, as for the EU area, is the Clinical Trials Regulation, replacing the previous directive on the matter. It entered into force in 2014, but its practical application depends on the development of a fully functional EU portal and database by the European Medicines Agency (EMA) together with the EU countries and the Commission, and therefore has been postponed to 2019[21].

The Regulation is designed to ensure a greater level of harmonization of the rules on conducting clinical trials throughout the EU[22]. It revolves around few basic principles: the need for a streamlined application procedure for all clinical trials conducted in Europe via a single EU portal and database; the idea that all applicants must be registered before assessment; the creation of a single authorization procedure for all

[17] Council of Europe official site, available at: https://www.coe.int/en/web/bioethics/oviedo-convention (last consulted 08/11/2018).
[18] Council of Europe official site, available at: https://www.coe.int/en/web/bioethics/oviedo-convention (last consulted 8/11/2018).
[19] Council of Europe official site, available at: https://www.coe.int/en/web/bioethics/oviedo-convention (last consulted 08/11/2018).
[20] Additional Protocol to the Convention on Human Rights and Biomedicine, concerning Biomedical Research available at: https://www.coe.int/en/web/conventions/full-list/-/conventions/rms/090000168008371a (last consulted 08/11/2018).
[21] https://ec.europa.eu/health/human-use/clinical-trials_en (last consulted 08/11/2018).
[22] https://ec.europa.eu/health/human-use/clinical-trials_en (last consulted 08/11/2018).

clinical trials, to allow a faster and more thorough assessment by all concerned EU countries; the extension of the silent agreement principle to the authorization process, giving more legal certainty to sponsors and researchers; the need to strengthen the level of transparency for clinical trials data[23].

These set of documents are the main basis of international regulations on human experimentation, equipping the medical science community with both prohibitions and guidelines to be followed by physicians and researchers alike.

4. The influence of inhuman experimentation in the past on the developing of international regulations

Before these rules were enacted and enforced, the international stage was almost completely unregulated: experiments were conducted rather freely on human beings, especially oppressed groups without so much as prohibitions on the type or the modalities of the experiments that could be carried out.

Experiments were mainly performed on slaves, minorities, prisoners of war during wartime or even inmates. These categories of outcasts were chosen mostly because the rest of the community did not care enough to object to experiments, even inhumane ones, conducted behind closed doors, and there was no regulation providing any kind of protection for these vulnerable groups of people.

For instance, experiments on convicted people were conducted even without consent, as if their participation to the research was to be considered part of the penalty. As for minorities and outcasts, especially those living in poor conditions, researchers often offered some kind of payment in exchange for the participation in the experimentation; alternatively, they appealed to hopelessly ill patients, willing to try anything in hopes for a cure. These experiments however, often did not have any therapeutic focus, but rather were carried out just for the sake of science and knowledge[24].

These unrestricted researches, as difficult as it is to admit it, led to scientific and medical discoveries of great magnitude that could only have been achieved through the means of human experimentation[25], even if the price to be paid was that of the lives of a great number of unfortunate people.

A striving example are the Nazis experiments on concentration-camps prisoners, mainly Jew, Gypsy and Slavic people, which were performed not only in the complete absence of any kind of international regulations or

[23] https://ec.europa.eu/health/human-use/clinical-trials_en (last consulted 08/11//2018).
[24] G.J. ANNAS, *op. cit.,* 121.
[25] L.K. ALTMAN, *Who goes first? The story of self-experimentation in medicine,* New York, 1987, 214.

prohibitions, but also with the State endorsement, whose "possessory interests" were enough to sacrifice individual rights[26]. The experiments, as highlighted by the trials, were conducted for purely scientific investigations, without regard to therapeutic advantage, and often it was well-known from the beginning that the result of such experiments would be death, or at least trauma, disfigurement or permanent disability. Even in the absence of international ethical codes, those experiments were still clearly in contrast with both German laws and the Code of Ethics of the German medical community, but the Nazis philosophy soon erased any kind of resistance, due to the premise of it all: prisoners were to be considered second-class citizens, whose rights could be overlooked[27].

These beliefs led to practices that went well beyond all reasonable ethical limits and were referred to as "medical tortures". The experiments included: injection of viruses to study the cure; experiments on twins; bones, nerves and muscle transplanting; freezing experiments; and experiments concerning different types of lethal gases. As previously stated, these experiments had hardly anything to do with therapeutic purposes and were purely carried out for the sake of scientific investigation and knowledge[28].

The Nuremberg Medical prosecutions, that followed WWII, offer the scientific and legal communities important lessons regarding the potential dangers to individual safety inherent in human experimentation, and the need for institutionalized controls to maintain a balance between advances in medical knowledge and the protection of individuals.[29] The involvement of the State in the Nazi practices also showed the need for an international set of rules above the power of the State, to protect at least a small amount of inalienable human rights, placed beyond the reach of national law and political power. These type of international prohibitions would protect even the weakest groups from the idea that «the end justifies the means», which often results in the failure of the state power or the scientific community in establishing effective laws on the proper conduct of scientific investigation. The Nuremberg Code worked, therefore, as a set of imperative rules based entirely on experience, to avoid the repeating of episodes as the ones from WWII, and to create guidelines for physicians and researchers: i.e. the Code stresses the importance of voluntary and informed consent, as a response to the coercion of prisoners into participating to clinical trials.

As for what concerns the Declaration of Helsinki and the Declaration of Geneva, they create a distinction between clinical research and "pure" clinical research, in order to include under the area of application of

[26] M. CHERIFF BASSIOUNI, T.G. BAFFES, J.T. EVRARD, *op. cit.,* 1606.

[27] "the subjects available to them were actually prisoners already scheduled for disposal by the State." INTERNATIONAL MILITARY TRIBUNAL, *The trial of German Major War Criminals: proceedings of the International Military Tribunal sitting at Nuremberg, Germany, Part 19, 16th July, 1946 to 27th July, 1946, taken from the original transcript,* 3rd Record, 1946.

[28] M. CHERIFF BASSIOUNI, T.G. BAFFES, J.T. EVRARD, *op. cit.,* 1606.

[29] M. CHERIFF BASSIOUNI, T.G. BAFFES, J.T. EVRARD, *op. cit.,* 1606.

the principles a wider spectrum of activities[3031]. The first is essentially therapeutic, while the second is performed primarily for the purpose of acquiring scientific information with little anticipated therapeutic value to the subject. Consequently, all types of research must follow the guidelines provided by the Declarations and must be conducted with respect to the life, health and privacy of the subject of the research, even if the research's purpose is not therapeutic.

The same goes for the Oviedo Convention, which aims to ensure that the interests of the individual outweigh the interests of society and science in general, in order to avoid situations like the Nazi experiments.

As for the Clinical trials Regulation, these provisions are developed to ensure that by following a strict procedure for the approval of clinical trials, the interests and safety of the subjects are fully respected.

In light of the enactment of these international regulations, the field of human experimentation is currently better regulated than it was in the past, as it is entirely based on informed and voluntary consent, and the respect of human life and health.

5. Self-experimentation: History & definition

Self-experimentation refers to the special case of a single-subject research, in which the experimenter performs the experiment on him/herself[32]: this usually means that a single person is the designer, operator, subject, analyst, and user or reporter of the experiment. Although, as previously stated, human experimentation has attracted intense study leading to a comprehensive legal and ethical framework of reference, the subcategory of self-experimentation has received much less attention[33].

Traditionally, the term self-experimentation identifies a situation where a physician or a researcher performs an experiment on him/herself rather than on a patient. In the past, this practice was widespread among medical researchers, for many different reasons: some did not want to endanger the patients' lives, trying a cure on them that had yet to be tested; sometimes the experiment did not meet the requirements for the official study; others wanted to convince the public that the cure was safe enough that the scientist who

[30] Declaration of Helsinki, available at: https://www.wma.net/policies-post/wma-declaration-of-helsinki-ethical-principles-for-medical-research-involving-human-subjects/ (last consulted 08/11/2018).

[31] Declaration of Geneva, available at: https://www.wma.net/policies-post/wma-declaration-of-geneva/ (last consulted 08/11/2018)

[32] https://en.wikipedia.org/wiki/Self-experimentation (last consulted 08/11/2018) and L.K. ALTMAN, *op. cit.,* 214.

[33] A.B. WEISSE, *Self-experimentation and its role in medical research,* in *The Texas Heart Institute,* 2012, 51-54 available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3298919/ (last consulted 08/11/2018).

created it was willing to try it; some wanted to prove that a particular disease had a virus basis rather than a psychosomatic one (see *infra*)[34].

Even though the reasons behind self-experimentation may have differed, the practice did follow a certain path that allows a marking of its outline. Despite just a few exceptions[35], most self-experimenters performed only a limited number of experiments on themselves, during a limited period of time, and usually in a specific field or for a particular purpose[36]: the practice did not amount to a generalized method of conducting a research, but rather a peculiar way to test its results, or a way to force it to move forward when it had met an impasse. Although there have been some episodes of self-experiments led by committees[37], the experiments are usually carried out by single individuals in relative isolation[38]. The research involved mostly revolves around infectious disease, in order to find proof of their infectious nature or to prove the cure/vaccine developed works; even so, there were also experiments regarding pharmacology, physiology, oncology and radiology.[39] It is to be noted that in the 89% of instances, the self-experiments obtained positive results in support of the hypothesis or valuable data that had been sought.[40]

In the remaining studies, in which the results were either negative or inconclusive, some of the negative results could also be viewed as beneficial in directing investigators into more fruitful avenues of research[41].

Of course, it was to be taken into consideration that the negative results could lead to the extremes of the death of the subject/researcher, or at least to severe illnesses and long-term disability[42].

The truth of the matter is that there were deaths as a result to self-experimentation, and of all the eight deaths of self-experimenters enumerated in *Table I*[43], only one of them is not the result of an infectious disease *(Bogdanov).*

[34] R. GHANI, *Self experimenting doctors*, in *British Medical Journal Careers*, 2011, available at: http://careers.bmj.com/careers/advice/view-article.html?id=20002566 (last consulted 08/11/2018).

[35] Some scientists have made self-.experimentation a continuing theme throughout their careers, using it as a basic tool in their scientific studies. Lawrence K. Altman analyses 4 of these cases in his book *Who goes first? The story of self-experimentation in medicine,* 1987.

[36] L.K. ALTMAN, *op. cit.*, 214.

[37] Walter Reed's Yellow Fever Commission in Cuba in 1900 to demonstrate the transmissibility of the disease through mosquitoes, see in A.B. WEISSE, *op. cit.,* 51.

[38] A.B. WEISSE, *op. cit.,*51.

[39] A.B. WEISSE, *op. cit.,* 52.

[40] A.B. WEISSE, *op. cit.,* 52.

[41] A.B. WEISSE, *op. cit.,* 52.

[42] A.B. WEISSE, *op. cit.,* 53.

[43] A.B. WEISSE, *op. cit.,* 53.

TABLE I Deaths from Self-Experimentation, 1800–1999

Year of Death	Person (Country)	Cause of Death
1817	Alois Rosenfeld (Austria)	Bubonic plague (?)
1849	Anthony White (United Kingdom)	Plague
1873	Otto Obermeier (Germany)	Cholera vaccine
1874	Joseph von Lindwurm (Germany)	Secondary syphilis
1885	Daniel Carrion (Peru)	Oroyo fever
1900	Jesse Lazear (United States)	Yellow fever
1920	Arthur Bacot (United Kingdom)	Typhus
1928	Alexander Bogdanov (Russia)	Multiple blood transfusions

These data show that, even if death is rather unlikely as a result of the injection of an untested cure/vaccine or the injection of an infectious disease, it clearly is one of the possible results. Especially in these cases, the lack of information, that can only be found by the means of clinical trials, made it impossible to foresee with certainty the results that the experiment might have had, and it still shows nowadays that the fact that death might be one of the ending point of this kind of research needs to be taken into account.

During the passing of time, the practice of self-experimentation has decreased in all fields of medical research (see *Table II*[44]), possibly because the approach to medicine and research has changed. The focus has in fact shifted, going from the acceptance of a single positive result, the one obtained with the experiment on the research, as enough to make the cure usable on a large number of people, to the need of statistically acceptable results, in order to legitimize the cure[45].

TABLE II Changing Trends in Self-Experimentation, 1800–1999

Field	1800–1849	1850–1899	1900–1949	1950–1999	Total
Infectious diseases	14	38	68	20	140
Anesthesiology	34	40	20	7	101
Physiology	10	19	51	21	101
Pharmacology	9	26	22	22	79
Radiology	—	—	22	7	29
Oncology	1	3	6	5	15
Total	68	126	189	82	465

5.1. Barry Marshall and the Helicobacter Virus

[44] A.B. Weisse, *op. cit.*, 52.

[45] A.B. Weisse, *op. cit.*, 54.

An example of self-experimentation involving infectious diseases is the case of doctor Barry Marshall and the *Helicobacter pylori.* Before the 20th century, ulcer was not considered a proper disease and the whole medical community was irretrievably convinced that the cause for it was stress.

Doctor Marshall, however, was certain that ulcers were caused by a bacteria infestation of the *Helicobacter pylori*, and could therefore be cured with simple antibiotics and acid secretion inhibitors, before turning into serious conditions such as peptic ulcers, or even stomach cancer[46]. The rest of the medical community responded in a very skeptical way, as such an idea defied the wisdom of the centuries which stated that the acid environment of the stomach could not possibly permit bacterial growth[47].

Marshall had no animal model that could prove *H pylori* was a pathogen. Being familiar with some of the famous self-experiments of doctors such as John Hunter's self-infection with gonorrhea and syphilis (which may have later caused his death), he decided to perform an experiment to prove his theory on himself with the help of his collegue Robin Warren. He expected to develop an asymptomatic infection, as it happens in the majority of the cases, and that would prove that anyone is susceptible to the bacterium, and consequently develop gastritis and eventually an ulcer later[48].

Marshall first underwent an endoscopy to confirm that he was negative for *H pylori*. Three weeks later he drank a broth made by his colleague, a suspension of two culture plates of the organism taken from a patient with dyspepsia (one of the consequences of gastritis), with confirmation that it was sensitive to metronidazole (the antibiotic to cure it).

After five days, he started to have bloating and fullness after the evening meal and his appetite decreased. His breath was bad and he vomited clear watery liquid, without acid, each morning at approximately 06:00 am. Then, a follow-up endoscopy showed severe active gastritis with polymorphonuclear infiltrate and epithelial damage. Evidently, *H pylori* was a pathogen that could affect everybody, proving that gastritis and ulcers were not caused by stress but rather came from bacteria[49].

The experiment took place in 1984, but both Marshall and Warren received the Nobel Prize for their discovery only in 2005: they were honored «for their discovery of the bacterium Helicobacter pylori and its role in gastritis and peptic ulcer disease». The Committee added, «thanks to the pioneering discovery by Marshall

[46] B. MARSHALL, P.C. ADAMS, *Helicobacter pylori: A Nobel pursuit?*, in *NCBI,* 2008, 895 available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2661189/pdf/cjg22895.pdf (last consulted 02/07/2018).

[47] R. LAKHTAKIA, I. BURNEY, *Self-Experimenting physicians, Mavericks or martyrs?*, in *NCBI,* 2015, 453 available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4664087/pdf/squmj1504-e452-455.pdf (last consulted 02/07/2018).

[48] B. MARSHALL, P.C. ADAMS, *op. cit.,* 895.

[49] B. MARSHALL, P.C. ADAMS, *op. cit.,* 896.

and Warren, peptic ulcer disease is no longer a chronic, frequently disabling condition, but a disease that can be cured by a short regimen of antibiotics and acid secretion inhibitors»[50].

This is therefore, a striking example of how self-experimentation was the last resort for the doctor to validate his theory. Furthermore, it is demonstrated how the positive results of the experiment influenced the entire medical community to the point of awarding the two doctors the Nobel Prize.

In the past, it was not uncommon that self-experiments led to Nobel-worthy discoveries (see *Table III*)[51], considering that they were performed by professionals who had spent a large amount of time developing the research that led to the experiment.

TABLE III Nobel Prizes Awarded to Self-Experimenters

Year	Recipient	Research Area
1903	Niels Finsen	Phototherapy
1904	William Ramsay	Discovery of inert elements*
1908	Elic Metchnikoff	Phagocytes*
1923	Frederick Banting	Insulin
1928	Charles Nicolle	Cause of typhus
1930	Karl Landsteiner	Blood types
1936	Victor Hess	Discovery of cosmic rays
1939	Gerhard Domagk	Sulfa drugs
1939	Ernest Lawrence	Cyclotron*
1943	George de Hevesy	Polarography*
1952	Albert Schweitzer	Humanitarianism*
1956	Werner Forssmann	Cardiac catheterization
2005	Barry Marshall	*Helicobacter pylori*

*Nobel prize awarded for work unrelated to self-experimentation.

The practice was wide-spread, mostly because in late 20th century medical practice landscape, ethical clearance for a human experiment was very difficult to come by. Consequently, researchers chose to experiment on a subject that was easy to find and whose consent was easily obtained: themselves.

For the kind of scientists whose work was not particularly risky, the main reason for choosing this practice over human experimentation on a previously approved set of subjects, is easily found: convenience[52]. Tests are easier on oneself and the collected samples do not institutional approval, obtain through long and tiresome procedures. As for consent, there is no need to worry about the subject retrieving it, or deciding to sue the researcher.

From this outline of self-experimentation in the past it can inferred that these experiments were performed solely by qualified personnel, who fully understood the research in its entirety and how it led to the experiment, and who consciously chose to undergo the experiment, being aware of the implications and the possible outcomes, including death. The researchers/subjects were also qualified enough to potentially put

[50] B. MARSHALL, P.C. ADAMS, *op. cit.*

[51] A.B. WEISSE, *op. cit.*

[52] E. LANDHUIS, *Do it yourself? When the researcher becomes the subject,* in *American Association for the Advancement of Science*, 2018, available at: http://www.sciencemag.org/careers/2016/12/do-it-yourself-when-researcher-becomes-subject (last consulted 08/11/2018).

an end to the experiment in case it turned bad. This panorama differs greatly to what self-experimentation is nowadays, in terms of subjects, purpose and approach to the practice (see *infra*).

6. A new approach to self-experimentation

Despite the fact that self-experimentation has developed into new different forms, it still remains a very unknown and unregulated phenomenon. The past approach is no longer wide-spread as it was, but it has not yet completely disappeared, as there are still people supporting it as a valid research technique.

An example might be the position of professor Rebecca Dresser who, in an exposition on the subject thereof, recognizes that self-experimentation was eventually replaced by human research, governed by more comprehensive ethical codes[53], but at the same time argues for its revival in a modified form.

She supports the practice mainly on the grounds of the accuracy of self-observation, the impossibility of complete replication of the human situation in animal models and the clear academic and moral arguments for «doing onto oneself before inflicting others»[54]. She also suggests that an element of leadership might be involved, as medical professionals can lead by example, before seeking informed consent from patients or healthy volunteers. Lastly, she notes that being involved in the trials may help physicians and researchers to better identify with the seriously ill patients that usually undergo these procedures.[55] However, she suggests that self-experimentation is to be done under the new regulations on human experimentation. Its use shall be avoided in cases of high risk interventions where the excitement and involvement of scientists in their research might lead to understatement of the hazards and burdens of the experiment. She therefore suggests the control of ethics committees, the use of modern peer review, regulatory and ethics review system, which might better single out which experiments can be performed with less risk[56].

Self-experimentation, as traditionally intended, started to be less popular as soon as the Nuremberg Code, the Helsinki Declaration and other research regulations were enacted and ethics review boards were created. Hence, it is very unlikely that, even as reformed as suggested, self-experimentation could be adapted to principles developed specifically with the intent of regulating human experimentation.

It can be inferred from the specific characteristics of self-experimentation, that even if researchers did request a formal approval through ethical committees before undergoing the practice, that approval would

[53] R. DRESSER, *Personal knowledge and study participation,* in *Journal of Medical Ethics,* 2014, 471–474, available at: https://www.jstor.org/stable/pdf/43283044.pdf?seq=1#page_scan_tab_contents (last consulted 08/11/2018).
[54] R. LAKHTAKIA, I. BURNEY, *op. cit.,* 453.
[55] R. LAKHTAKIA, I. BURNEY, *op. cit.,* 453.
[56] R. DRESSER, *op. cit.,* 471-471.

be really hard to obtain, due to the legal implications. Given that some experiments may potentially be equated with suicide, an approval of a formal committee might imply some degree of responsibility that no ethics committee would undertake. Yet, if the experimenters do survive to tell their tale, the scientific community invariably embraces the new discoveries, as it always did in the past, and that could encourage researchers not to seek the previous approval, but rather settle for an *a posteriori* recognition[57]. Dresser claims that a valid alternative might be to simply demand a different and less skeptical attitude from the leaders of research teams towards their mentees' idea, so that they would be able to prove their theories through approved experimentation rather than self-experimentation[58].

However, researchers might as well decide to undergo self-experimentation anyway to prevent an original idea from being plagiarized, so the problem would not be completely solved just by inserting a formal approval of self- experiments.[59] For now, it is left to researchers to decide whether they are comfortable experimenting on themselves and whether they need to seek the ethics committee approval[60], as there is no enacted law preventing them to perform the experiment without any kind of authorization.

Other reasons why self-experimentation is not quite as common as it was before, mostly revolve around the changes in the field of medical research. First of all, there are the blatant ethical concerns: injecting oneself with untested cure, the widest form of self-experimentation nowadays, is deemed reckless and generally the potential benefits are considered as not worth the risk. As far as drugs and vaccines go, their public distribution is now subjected to a long approval process that involves different phases, carried out by following data collections protocols and in a randomized and blinded manner: they consist in experiments on animals and on largely diverse samples of human subjects; the data analysis and evaluation of findings is usually subjected to a proper peer-review and therefore can legitimize the product of the research[61].

The procedure possibly followed by a physician or researcher injecting himself, even a very attentive one, inherently lacks some of these characteristics: the statistical validity given by the performance of the test on a sample of subjects with different characteristic, rather than just one subject; the randomization and blindness of the experiment. Lastly, the experimenter's personal involvement and motivation in the project inevitably make the research seem less objective. Therefore, the results, even the positive ones, do not

[57] R. LAKHTAKIA, I. BURNEY, *op. cit,* 454.
[58] R. DRESSER, *op. cit.,* 471-471.
[59] R. LAKHTAKIA, I. BURNEY, *op. cit.*, 454.
[60] E. LANDHUIS, *op. cit.,* 1.
[61] R. DRESSER, *op. cit.,* 471-471.

provide the research with the same scientific legitimacy that the institutionalized clinical trials might provide[62].

Other physicians and researchers, such as professor John Saunders, chairman of the Committee on Ethical Issues in Medicine at the Royal College of Physicians, support the practice of doctors taking part in their own approved clinical trials. According to him, there is no ethical reason why doctors should not be able to participate in their own approved trials, as he did. However, he decisively stresses that this is only valid for approved experiments, and not for unauthorized self-experiments: in his research he was not the sole volunteer, he was taking part in it as any other experimental subject; and he should therefore not be excluded from the trial on the sole basis of being an investigator in the research[63]. Even so, other doctors such as Darryl Reese, chair of Cambridgeshire 1 Research Ethics Committee, argue that even in these cases, objectivity cannot be guaranteed, as the researcher is too involved: double blind studies and placebo controls were introduced to avoid bias, but the involvement of the doctor removes the benefits that these mechanisms provide.

6.1. The "common" self-experimenter

Despite all the arguments listed above, the practice of self-experimentation has survived, albeit in different forms, with different subjects, purposes and methods.

As for what concerns the subjects, experiments are not performed only by physicians or researchers anymore, but also by "common people" without any training in the field. These new practitioners belong to two emerging categories: "common" people who have a life-threatening disease/condition and because of it are willing to try untested cures; "biohackers" and members of organizations such as Quantified Self, which «supports new discoveries about ourselves and our communities that are grounded in accurate observation»[64], through the means of self-experimentation. According to the main internet site, Biohackers experiment with the purpose of «taking control of their own biology, and manipulate the environment outside and inside themselves so they can program it to perform at any level they want and supercharge results»[65].

As a matter of fact there are actually two approaches to biohacking: one refers to biology in general, outside of the human body, and consists in trying to make «biology accessible to everybody "hacking" it, and breaking

[62] R. LAKHTAKIA, I. BURNEY, *op. cit,* 454.
[63] R. GHANI, *op. cit.,* 1.
[64] http://quantifiedself.com/about/ (last consulted 08/11/2018)
[65] http://www.biohackers.global/ (last consulted 08/11/2018)

the monopoly of the "Big Bio", the big operators in biology sciences to make them inclusive»[66]. The second one is based on the idea that «you can hack your own biology, and you can gain control of systems in your body, that you would never have access to»[67]. The latter is the approach that involves self-experimentation, with a range that goes from simple control of the eating regime and self-observation to self-injections of untested treatments. As it can be inferred, these days self-experimentation mainly revolves around the testing of unapproved treatments on oneself, therefore largely dismissing experimenting to prove the nature of infectious diseases, as it was done in the past.

6.2. Case 1: Aaron Traywick injects himself with herpes experimental cure

A striking and worrying example is the case of Aaron Traywick, CEO of Ascendence Biomedical, who took the stage at a biohacking conference in Austin, Texas on February 4th 2018 and injected himself in the thigh with an experimental herpes treatment created by his company. The "cure" consisted in «live attenuated herpes virus with a missing protein»[68], and as Traywick claims, should have «the potential to allow individuals, without the requirement of a clinician or without the healthcare industry, to be able to self-design and self-administer treatments»[69]. The self-experiment was broadcasted on Facebook Live, and it is not the first stunt pulled by biohackers who, despite having limited or no medical experience, are creating alleged treatments from DNA strands they order on the internet.

6.3. Case 2: Josiah Zayner injects himself with muscle enhancer

A similar story is the one of another famous biohacker, Josiah Zayner CEO of ODIN, who publicly injected himself with DNA encoding for CRISPR that could theoretically enhance his muscles, live-streaming it all during a conference. Despite its own stunt, which he now regrets, Zayner does not approve Traywick's gesture, as what was meant to be provocative, is now spreading and could result in somebody getting hurt

---

[66] A. DI CORINTO, *Biohacker, ecco chi sono gli hacker della vita,* in *Wired,* 2015, available at: https://www.wired.it/economia/lavoro/2015/02/07/biohacker-gli-hacker-vita/ (last consulted 08/11/2018).

[67] S. MICHELS, *What is biohacking and why should we care?*, in *PBS*, 2014 article on Dave Asprey, available at: https://www.pbs.org/newshour/science/biohacking-care (last consulted 08/11/2018).

[68] E. MULLIN, *A biotech CEO explains why he injected himself with a DIY herpes treatment on Facebook Live,* in *MIT Technology Review,* 2018, available at: https://www.technologyreview.com/s/610179/a-biotech-ceo-explains-why-he-injected-himself-with-a-diy-herpes-treatment-live-on-stage/ (last consulted on 08/11/2018).

[69] E. MULLIN, *op.cit.,* 1.

eventually. He even goes so far as discouraging people to buy the untested treatments that his company produces, just to inject themselves, rather than study them[70].

Experts, such as the American Society of Gene & Cell Therapy (ASGCT), the largest professional society representing gene and cell therapy in the world, do not support the practice of injecting unregulated gene therapies, because such procedures are potentially dangerous and highly unlikely to provide therapeutic benefits[71]. Therefore these "do-it-yourself" gene therapies are strongly discouraged, as they are in no way proven safe nor effective, and they are not the result of rigorous scientific and clinical research.

6.4. The FDA response

The US Food and Drugs Administration (FDA) did not comment directly on the Ascendance event, but in a statement claimed that, in order to test unapproved drugs on humans, an investigational new drug application must be submitted to the Agency and become effective, before the drug can be tested. Therefore, these DIY gene-therapies are to be considered illegal.[72] Ascendance and ODIN claim that their activities are legal as everything is labeled as «not for human consumption, technically»[73], implying that it is up to the buyers to decide what to do with the components.

As the interest in biohacking is spreading, it is becoming increasingly easier for the interested parties to obtain on the internet both the DNA samples and the procedures necessary to carry out gene editing using CRISPR. Nonetheless, ODIN claims that the components they sell cannot be directly used to alter a person's genes as they need to undergo a few other steps to be ready for use, ensuring that the person possibly injecting him/herself is at least somewhat competent.

At the same time, this is evidently not an approach endorsed by every company in the field as there are completed cures, even though still untested, that are available on the market for direct use. An example of these companies is Ascendance which promotes decentralized testing for new drugs[74]. Despite the warning of the FDA and not having the agency permission to experiment on humans, Traywick, CEO of the aforementioned company, thinks that the decentralized experiments are not illegal because they are not

[70] S. ZHANG, *A Biohacker Regrets Publicly Injecting Himself With CRISPR,* in *The Atlantic,* 2018, available at: https://www.theatlantic.com/science/archive/2018/02/biohacking-stunts-crispr/553511/ (last consulted 08/11/2018).

[71] ASGCT Board of Directors, *ASGCT Statement on DIY Gene Therapy,* in *American Society of Gene & Cell Therapy,* 2017 available at: https://www.asgct.org/research/news/december-2017/asgct-statement-unregulated-diy-gene-therapy (last consulted 08/11/2018).

[72] E. MULLIN, *Biohackers Disregard FDA Warning on DIY Gene Therapy,* in *MIT Technology Review*, 2017, available at: https://www.technologyreview.com/s/609568/biohackers-disregard-fda-warning-on-diy-gene-therapy/ (last consulted 08/11/2018).

[73] E. MULLIN, *A biotech CEO explains why he injected himself with a DIY herpes treatment on Facebook Live,* cit.

[74] E. MULLIN, *Biohackers Disregard FDA Warning on DIY Gene Therapy,* cit.

charging for the experimentation and they are not «providing a compound and marketing a compound for a specific health purpose and providing it for sale»[75], as the therapy is offered for research purpose only.

6.5. Case 3: Tristan Roberts and the HIV cure

The research purpose Traywick refers to, includes also the case of Tristan Roberts, an HIV patient who was filmed live on Facebook while injecting himself with a gene therapy designed to generate antibodies that he believed would help his body destroy cells infected with the virus.

Roberts and Traywick, who was there with him at the time, both identify as biohackers and have no formal training in medicine or genetic engineering. Roberts was diagnosed with HIV earlier in life but stopped taking conventional antiretroviral drugs due to side-effects and the fact that he did not want just a temporary remedy to his disease, but rather a ultimate one in order to be cured once and for all. Therefore, he decided to inject himself with the gene therapy designed by Ascendance Biomedical to produce N6 antibodies, coming from one of the few patients who had defeated the virus on their own. The therapy was based on a US National Institutes of Health (NIH) study which showed how N6 neutralised 98% of the HIV virus in lab conditions[76]: this, however, has not yet been transformed in a cure by means of institutionalized research, nor has any potential treatment been tested or approved by the FDA. These biohackers' goal is to create a cure for HIV outside of the institutional medical environment and provide it to HIV patients in a cheaper and faster way than what would be possible following the standard procedure.

Many scientists and bioethicists argue that experiments like this one are seen as too amateur to produce any meaningful results and the dangers of self-experimentation outweigh the potential benefits. Also, patients who try self-experimentation may have no idea what they're signing up for[77].

«I strongly fear that, without a robust structure for conducting risk-assessment and handling risk and liability issues, the Ascendance Biomedical model will only transfer all these heavy, complex responsibilities to individuals at their own cost and peril»[78] wrote Eleonore Pauwels, a science policy expert at the Woodrow Wilson International Center and a genomics specialist. Now more than ever, people like Roberts can play in a genetic arena that was once strictly reserved to professionals, since at the moment anyone can obtain a

[75] E. MULLIN, *Biohackers Disregard FDA Warning on DIY Gene Therapy,* cit.

[76] J. LUSSENHOP, *Why I injected myself with an untested gene therapy*, in *BBC NEWS*, 2017, available at: https://www.bbc.com/news/world-us-canada-41990981 (last consulted 08/11/2018).

[77] J. LUSSENHOP, *op.cit.,*1.

[78] J. LUSSENHOP, *op. cit..,*1.

custom gene sequence with the ease and convenience of online shopping. The FDA response, condemning unlicensed human testing and the sale of gene-editing products or kits intended for self-experimentation as against the law, was not enough: whether or not self-administering an untested drug is illegal still remains a grey area that amateur scientists and biohackers are eagerly taking advantage of[79].

During the weeks following the injection, Roberts suffered from side-effects that could be related to it, even though he was not certain and the results of the experiment were not as groundbreaking as he and Traywick expected: his viral load rose from 28,800 on week two to 36,401 on week three - still low levels, but not the desired results. His count of CD4 helper T-cells - the immune system cell that HIV attacks - was higher than he would ever seen it, but there was no way to know what that meant[80]: at best, the "cure" did not make the virus stronger. Mark Connors, the lead NIH scientist who discovered the antibody used for this experiment, was not surprised by the results as he already claimed that the antibody could not wipe out the virus all on its own. He also highlights the raging debate in the field about whether or not antibodies alone will ever be able to cure the virus: HIV protein envelope continuously mutates, shifting into forms that prevent our antibodies from binding to and neutralising it. As potent as N6 is, HIV can still develop a resistance to it, making it a poor candidate as a "monotherapy" or stand-alone treatment, said Connors. He added that «for the most part, the rules aren't what take so long [in drug development], it's not the FDA sitting on drugs. The reality is, this is a deliberative process».[81]Even the actual developer of the treatment inside Ascendance, who has remained anonymous, does not agree with defining it as a definitive cure, nor with its use in Roberts' self-experimentation. Because of this kind of behaviour, other self-experimenters refuse to identify as biohackers, insomuch their actions are often very reckless and they disparage the practice of self-experimentation in the eye of the public.

Among these is Brian Hanley, a microbiologist who gave himself a gene therapy designed to increase his stamina and life span: while he agrees with scientists and professionals experimenting on themselves, he fears that the activities of biohackers who promote self-experimentation will encourage total amateurs to take risks they cannot possibly understand. «They could give themselves a significant issue, potentially including dying from it, [...] the biggest danger is you could infect yourself with something»[82].

[79] J. LUSSENHOP, *op. cit..,*1.
[80] J. LUSSENHOP, *op. cit..,*1.
[81] J. LUSSENHOP, *op. cit.,* 1.
[82] J. LUSSENHOP, *op. cit.,* 1.

The outline of these experiments shows that, nowadays, the practice of self-experimentation poses problems on different levels, some shared with the old practice and some completely new. They can be summarized in 4 main areas: practicality, accuracy, reliability and ethics[83].

7. Self-experimentation criticalities: practicality

A strong argument against self-experimentation is the complete lack of institutional involvement and, in light of that, also the absence of a competent professional able to stop the experiment in the event of grave life-threatening complications. If the experimenter has no training in any field relating medicine (see *Tristan Roberts*), he/she is decisively not qualified to perform the experiment itself nor to stop any unforeseen complications that might arise.

However, even if the subject performing the experiment is a qualified researcher, it cannot be ensured that during the course of the experiment he will be able to stop it, especially if the unexpected complications are extremely grave, which explains the several deaths due to self-experiments in the past (see *supra*)[84].

The counterargument used by advocates of the practice revolves around this consideration: when the research does not pose any immediate and grave risk to the health of the researcher, it might be convenient for him/her to experiment on him/herself. For instance, it is much easier to analyse one's own blood, rather than to gather samples from people who need to give their informed consent, at the risk of it being withdrawn later. Additionally, as there are no official procedures or protocols to be followed, it is faster than experimenting on other subjects. However, this argument is now weaker because, if in the past self-experimentation was much faster than normal clinical trials due to the difficulty in finding volunteers, the situation today is considerably different: not only finding volunteers is easier and faster thanks to technology, but also accessing the kind of information needed for valid consent is.

7.1. Accuracy problems

As for what concerns accuracy, the involvement of many researchers and physicians in the different phases of the clinical trials ensures professional control on every aspect of the experiment: before, during and after the proper testing. Hence, considering the ontological complexity of most experiments, the documentation of the latter cannot be as accurate if the research and the experiments are carried out only by one person,

[83] R. GHANI, *op. cit.,* 1.

[84] A.B. WEISSE, *op. cit.,* 53.

which is also the test subject[85]. Thus, even if the results of a single experiment were enough to lead to a monumental discovery, the lack of institutionalized control, or at least the participation by a certain number of experts in the testing, defies the accuracy of the results[86]. In a field defined by the idea that the results of an experiment must be replicable in the future just to be taken into consideration, the choice of one time experiments whose accuracy can be questionable, rather than clinical trials, is less likely to be considered justifiable.

7.2. Reliability problems

Another pressing problem is the one of the reliability of the results of self-experimentation. The lack of institutionalized controls, pre-approved procedures and protocols deprives the research of strong legitimizing elements. Adding to this the fact that the researcher is also the subject and, therefore, thoroughly involved, it is strongly suggested that the results cannot be considered objective.

For these reasons, authors like JK Davis claim that except in certain cases of unusual risk, self-experimentation should not be encouraged: it is scientifically inadequate for its lack of proper controls and sufficient subjects to generate meaningful results[87].

Indeed, as far as medical research is concerned, the lack of a large and diversified subjects pool defies the reliability of trials' results: procedures for the approval of new drugs (i.e. FDA Development & approval process for drugs, see *infra*) are carried out through clinical trials that involve several hundreds of volunteers, healthy and affected by the disease, to ensure the statistical validity of the results. Thus, one subject-experiment are barely reliable.

7.3. Ethical problems

Ethically speaking, supporters of self-experimentation argue that there is a moral need to go first when experimenting a potential treatment: how can researchers expect others to try what they are not willing to try firsthand?

Even if the experiment is at high risk, and maybe even more so in these cases, most researchers might that experimenting on themselves may help legitimize what they are studying, or, at least, be a catalyst for further

[85] R. GHANI, *op. cit.,* 1.

[86] R. GHANI, *op. cit.,* 1.

[87] J.K DAVIS, *Self Experimentation*, in *NCBI Publication Medical*, 2003 available at: https://www.ncbi.nlm.nih.gov/pubmed/14979319 (last consulted 08/11/2018).

research[88]. Additionally, advocates adamantly claim that self-experimentation does not violate any ethical or moral rule: experimenting on oneself is widely inside the boundaries of self-determination, according to which everyone is entitled of their own person and can do what they want to do with their body.

Nonetheless, while in theory individuals are free to do what they like to themselves, Professor John Saunders thinks that there are other aspects to consider: we have responsibilities to each other and it is relatively unusual that one can claim that knowledge can only be reached by self-experimentation.

The answer could be to balance the pursuit of knowledge with other responsibilities: «I think that there is a point at which we say the price for new knowledge may be so high that it conflicts with other values that we have as a society. I think just saying, oh well this is the only way we can find this out—and it often isn't—[but even] if that is true it is not automatically justified. It just means that scientific progress may be a bit slower» says Saunders[89].

Ethical problems may arise also whilst dealing with informed consent: the supporters of self-experimentation argue that in these cases the author is both experimenter and single subject, so the requirement for informed consent does not apply. However, it should be considered that, if the experimenter is not a scientist/researcher, he has little to no knowledge about the content of the treatment and does not fully comprehend the possible outcomes of the experiment (see *infra*).

8. Self-experimentation and international regulation

The main problem concerning self-experimentation remains however the one of regulation: even though the situation is serious and spreading at alarming rates, it is mainly not addressed by international regulations.

Throughout this analysis it has been assessed how international regulations such as the Nuremberg Code and the Declaration of Helsinki are applied to human experimentation in general, but how may theu be applied specifically to self-experimentation?

Except for one specific mention of the practice in Article 5 of Nuremberg Code, the phenomenon is largely overlooked by international regulations, mostly concerned with non-consensual harmful research on vulnerable minorities. Besides, even when addressed, self-experimentation is not limited but rather allowed, as an exception to the general ban on experiments that present an *a priori* reason to believe that death or

[88] R. GHANI, *op. cit.,* 1.

[89] R. GHANI, *op. cit.,* 1.

disabling injury will occur, «except, perhaps, in those experiments where the experimental physicians also serve as subjects» (art.5)[90].

This exception, although questionable, was necessary at the time: the prosecutor at Nuremberg (and apparently the judges as well) thought that this would prevent the Nazi doctors from arguing that previous US government military experiments — most notably the Walter Reed yellow fever one[91] — had also knowingly risked the lives of subjects. This explanation is supported by the originally suggested wording of Article 5 by each of the two principal doctors who worked for the prosecution at Nuremberg, Leo Alexander and Andrew Ivy, who wanted to go as far as explicitly quoting the experiment[92]. Even so, it is possible to find principles in these international regulations on human experimentation, although not always legally binding, that may also apply to self-experimentation.

Starting with the Nuremberg Code, the necessity of consent is clearly implicitly fulfilled when the experimenters is also the test subject, but it is safe to say that it may not always qualify as fully informed consent as it is required. The realm of self-experimentation must be divided in two areas: the experiments performed by physicians or researchers on themselves; and those performed by non professional, such as biohackers, lacking training in any scientific field, that are injecting themselves with cures developed by other subjects, that are not supervising the experiment.

In the first case, more common in the past, it should be noted that consent is clearly informed, as the subject of the experiment is most likely the developer of the research behind the procedure that is to be carried out.

In the second case, on the contrary, the subject undergoing self-experimentation is not a qualified expert but rather a "common" person who most likely bought the cure online and has no scientific knowledge that might ensure the understanding of the implications of such a practice. Thus, consent, although present, is not informed as required and therefore not valid.

Furthermore, in these type of situations the experiment is not conducted by scientifically qualified people, as principle number 8 of the Code requires, and therefore no «scientist in charge prepared to terminate the experiment at any stage if there is probable cause to believe [...] that a continuation of the experiment is likely to result in injury, disability, or death to the experimental subject»[93].

---

[90] Article 5 of the Nuremberg Code available at: https://history.nih.gov/research/downloads/nuremberg.pdf (last consulted on 08/11/2018).

[91] Walter Reed's Yellow Fever Commission in Cuba in 1900 to demonstrate the transmissibility of the disease through mosquitoes, see in A.B. WEISSE, *op. cit.,* 51.

[92] G.J. ANNAS, *Self experimentation and the Nuremberg Code,* in *British Medical Journal*, 2010, 341, available at: https://www.bmj.com/content/341/bmj.c7103.full (last consulted 08/11/2018).

[93] Principle 10 of the Nuremberg Code available at: https://history.nih.gov/research/downloads/nuremberg.pdf (last consulted on 08/11/2018).

Moving to the Declaration of Helsinki, it is found that the latter does not comment on self-experimentation, as it is concerned prominently with research in patients and healthy volunteers, carried out by professionals[94]. Because of this focus, it can be said that the Declaration was not intended to prevent people from performing and reporting self-experimentation[95]. Nevertheless, as self-experimentation is just a branch of the experimentation field, some of the basic principles could be applied analogically.

Advocates of the practice stress that the Declaration grants the subjects of the research the right to self-determination, as long as their decisions are voluntary and the consent given is informed, without specifying that the subject of the research must be different from the individual performing the experiment. The counter argument relies on the same premises as the one approaching the necessity of informed consent required by the Nuremberg Code (see *supra*).

The Declaration of Helsinki also imposes a series of obligations concerning the operational aspects of the experimentation process: «Research should be based on a thorough knowledge of the scientific background (Article 11), a careful assessment of risks and benefits (Articles 16, 17), have a reasonable likelihood of benefit to the population studied (Article 19) and be conducted by suitably trained investigators (Article 15) using approved protocols, subject to independent ethical review and oversight by a properly convened committee (Article 13)»[96].

According to these principles, self-experimentation should be carried out only after receiving the approval of the committee and only by professional physicians following approved protocols.

The same principles are replicated in the Oviedo Convention, which, although not specifically intended to regulate self-experimentation, might be applied to the practice, as it concerns «research activities in the health field involving interventions on human beings»[97], regardless of the subject performing the experiment. The Convention subjects the possibility of carrying out a certain research to an authorization of a competent body, to be determined by each State, and of an independent ethics committee to ensure that the benefits of the research outweigh its potential risks. This however, requires data that are more easily collected if the

[94] L.E. BRYANT JR. *op. Cit,* 19-20.

[95] Case commitee on publication ethics site, available at: https://publicationethics.org/case/ethics-self-experimentation (last consulted 08/11/2018).

[96] Declaration of Helsinki, available at: https://www.wma.net/policies-post/wma-declaration-of-helsinki-ethical-principles-for-medical-research-involving-human-subjects/ (last consulted 08/11/2018).

[97] Oviedo Convention, available at: https://www.coe.int/en/web/conventions/full-list/-/conventions/rms/090000168008371a (last consulted 08/11/2018).

research follows strict procedures and guidelines, under the control of specific institutions: all these elements are absent in self-experimentation as it is today.

The last document mentioned above is the Clinical Trials Regulation, which aims at ensuring a greater level of harmonization of the rules on conducting clinical trials throughout the EU, by requiring, among other things, a single authorization procedure for all clinical trials, to allow a faster and more thorough assessment by all concerned EU countries[98].

Taking into consideration the cases analyzed throughout this exposition, it can be inferred that in no case these principles were followed. It is easy to understand the underlying reasons: the main argument for self-experimentation is convenience, and the need to develop protocols and obtain the approval of an ethical committee ontologically defies this argument. Moreover, it is very unlikely that an ethical committee would approve a research based entirely on self-experimentation: it presents all the critical issues outlined above and provides the research with close to no reliability. Additionally, as most of the subjects are not trained in any field relating medicine, their "research" does not follow the typical course that would allow them to present requests for approval of their clinical trials by an ethical committee; also, they explicitly claim not wanting to conform to the typical medical research procedure[99].

All these documents endorse the argumentation of some experts such as Rebecca Dresser, according to whom if self-experimentation shall be allowed, it would need to be performed following strict procedures, including the need for the approval of the Institutional Review Board (IRB) or other ethics committee[100]. As a consequence, publication of any self-experimentation research carried out by an independent researcher would not be allowed, because of the lack of access to any ethics committee or IRB: historically speaking, however, this would have prevented the publication of highly useful reports achieved outside the institutionalized process (see Barry Marshall, *above*).

Even though some of the provisions of the Convention and the Clinical trials Regulation might apply to self-experimentation as well, these documents were not developed to regulate this practice, and therefore some of the principles in them conflict with it. Notably, the Convention stipulates that «research on human beings may only be undertaken if there is no alternative of comparable effectiveness» (Article 5)[101].

[98] https://ec.europa.eu/health/human-use/clinical-trials_en (last consulted 08/11/2018).

[99] E. MULLIN, *A biotech CEO explains why he injected himself with a DIY herpes treatment on Facebook Live,* cit.

[100] Case commitee on publication ethics site, available at: https://publicationethics.org/case/ethics-self-experimentation (last consulted 08/11/2018).

[101] Oviedo Convention, available at: https://www.coe.int/en/web/conventions/full-list/-/conventions/rms/090000168008371a (last consulted 08/11/2018).

Institutionalized clinical trials are ontologically an alternative of comparable effectiveness to self-experimentation, and a rather better one, providing the possibility to draft more easily an evaluation of the risks and benefits, as required by article 6 of the Convention[102].

As for the Clinical trials Regulation, one of the main principles it is based on, is the need for the transparency for clinical trial data, which is unlikely to be achieved in a completely non institutionalized practice such as self-experimentation, which lacks entirely of external oversight and objectivity, due to the involvement of the experimenters, that might ensure transparency of the data collected.

For the reasons mentioned above, none of the documents analyzed provide a certain and clear legal framework of self-experimentation: the Convention and the Clinical Trials Regulations only present some guidelines that could be applied analogically; neither the Nuremberg Code nor the Declarations of Helsinki and Geneva provide an unequivocal frame of reference, being developed to regulate human experimentation.

Lastly, the Declaration of Geneva, being an oath reserved to physicians and researchers, it does not apply to "biohackers", namely the main advocates for the practice, who are in no way professionals.

Accordingly to this picture, supporters of self-experimentation maintain that this unregulated practice is well within the boundaries of self-determination, as in the right to decide what to do with one's own body. As such, this fundamental freedom should not be limited by a legal or ethical framework, leaving it up to researchers to weigh practicality against ethical considerations.

9. Right to try laws & self-experimentation

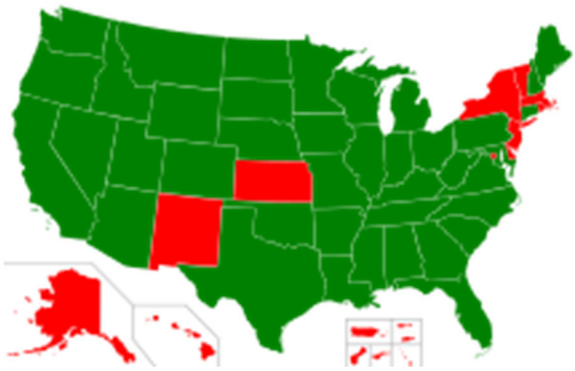
The topic of Right to Try laws might *prima facie* seem unrelated to self-experimentation, as the beneficiaries of the right to try are not experimenting on themselves. However, as these subjects are exercising what could be seen as right of self-determination, they are in a similar position to the one of people experimenting on themselves. By choosing, as allowed by the right to try laws, to undergo an experimental treatment they are essentially deciding to experiment an unapproved drug on themselves. They are becoming subjects of a research that is still pending with the consciousness that the results of this "experiment" might not be what they are expecting: the drug might, at best, be ineffective; at worst, it might worsen the disease/condition.

[102] Oviedo Convention, available at: https://www.coe.int/en/web/conventions/full-list/-/conventions/rms/090000168008371a (last consulted 08/11/2018).

The substantial difference with the practice of self-experimentation, which involves completely untested drugs, is that drugs that have passed Phase 1 of the FDA approval process have already been tested to evaluate the toxicity of the drug. Therefore, this kind of "allowed self-experimentation" resulting in death is very unlikely. However, considering that safety data are collected up to phase 4, many experts and critics argue that Phase 1 might not be enough to declare the drug safe enough to grant access to it to patients, even under their "Right to try" (see *infra*).

9.1. Right to try laws

Right to Try laws are US state laws that allow «terminally ill Americans to try medicines that have passed Phase 1 of the FDA approval process and remain in clinical trials but are not yet allocated among the public, therefore anticipating the possibility to access potentially life-saving treatments years before patients would normally be able to access them»[103].



In May 2014, Colorado became the first state to pass a Right to Try law. As of June 2018, 40 states have enacted such laws: Alabama, Arizona, Arkansas, California, Colorado, Connecticut, Florida, Georgia, Idaho, Iowa, Illinois, Indiana, Kentucky, Louisiana, Maine, Maryland, Michigan, Minnesota, Mississippi, Missouri, Montana, Nebraska, Nevada, New Hampshire, North Carolina, North Dakota, Ohio, Oklahoma, Oregon, Pennsylvania, South Carolina, South Dakota, Tennessee, Texas, Utah, Virginia, Washington, West Virginia, Wisconsin, and Wyoming (*in green in the picture*)[104].

Right to try laws are applied in different ways in accordance with the divergence of the state laws; however, a common feature is the fact that they all allow patients, doctors and drug companies to decide whether a patient has access to a drug that is still being tested in clinical trials, if certain requirements are met. The requirements change according to the state law, but they are similar to the compassionate use federal requirements (see *infra*).

Negotiation about passing a federal right to try bill started in January 2017, but only on March 21, 2018, the House of Representatives passed a right to try bill, sending it to the Senate for consideration.[105] On May 22nd,

[103] Right to try official site available at: http://righttotry.org/faq/ (last consulted 08/11/2018).
[104] Right to try official site available at: http://righttotry.org/faq/ (last consulted 08/11/2018).
[105] S. KARLIN-SMITH, *House passes right-to-try bill on second try*, in *Politico*, 2018.

the Senate passed the bill, and it was then sent to the President's desk for his signature[106]. On May 30th, President Trump signed the bill into law[107].

This federal law will essentially extend on a federal level the content of the states law granting terminally ill patients the right to seek drug treatments that remain in clinical trials and «have passed Phase 1 of the Food and Drug Administration's approval process» but have not been fully approved by the FDA[108]. For people living in a state where right to try state laws were already enacted, the scenery will not drastically change, but for people living in the 10 states without such legislation, this federal law will enable them to work with their doctors directly to approach a drug company with a drug in clinical trials and ask for the option to try that drug outside of the clinical trial[109]. This law eliminates the application requirements to the FDA, and creates a background harmonized on a federal level, overcoming critics on the potential unconstitutionality of state laws in matters of federal competence.

9.2. The FDA Development & approval process for drugs

In order to understand the significance of the approval of these laws in the field of human experimentation, an analysis of the "Development & Approval Process" for new drugs is needed. This process was developed by the FDA and supervised by the FDA's Center for Drug Evaluation and Research (CDER).

Drug companies seeking to sell a drug in the United States must first test it, to achieve two "goals": the first is to learn whether the treatment works well enough, and it is called "efficacy" or "effectiveness"; the second is to learn whether it is safe enough, and it is called "safety". Neither is an absolute criterion; both safety and efficacy are evaluated relatively to how the treatment is intended to be used, what other treatments are available, and the severity of the disease or condition. The outline is that the benefits must always outweigh the risks[110], and in order to do so the drug review process enables testing it from different approaches to ensure that all the requirements for distribution among the public are fulfilled. Before testing a drug on people, researchers must test it in preclinical studies, to determine its toxicity, as in the potential to cause serious harm. This research can be carried out in two ways: in vitro or in vivo[111]. Although these studies are

[106] M. TOMOSKI, *Trump To Sign Bill Which Could Make Cannabis Federally Legal For The Terminally Ill*, in *Herb.co*, 2018.
[107] J. HELLMANN, *Trump signs 'right to try' drug bill*, in *The Hill*, 2018.
[108] Right to try official site available at: http://righttotry.org/faq/.
[109] https://edition.cnn.com/2018/03/22/health/federal-right-to-try-explainer/index.html (last consulted 08/11/2018)
[110] US FDA official site, *FDA's Drug Review Process*, available at: https://www.fda.gov/Drugs/ResourcesForYou/Consumers/ucm289601.htm (last consulted 08/11/2018).
[111] https://mpkb.org/home/patients/assessing_literature/in_vitro_studies (last consulted 08/11/2018).

not very large, they must provide detailed information on dosing and toxicity levels, in order to decide if the drug should be tested on people[112]. While preclinical research allows the research to go further, the process to ensure drug's safety and effectiveness cannot disregard the need for trials that involve human beings: the clinical research phases. These trials are modeled on specific research questions related to the drug and therefore follow a protocol, usually developed by the researcher/manufacturer. These protocols must contain different information depending on the purpose of the phases, and focus on: the selection criteria, the number of candidates, the duration of the trials, ways to limit research bias, the modalities and dosage used during the testing, the kind of data that will be collected and how they will be review and analyzed[113].

Drug developers, or sponsors, must submit an Investigational New Drug (IND) application to FDA before beginning clinical research. In the IND application, developers must include: animal study data and toxicity (side effects that cause great harm) data, manufacturing information, clinical protocols (study plans) for studies to be conducted, data from any prior human research, information about the investigator.

The FDA review team has 30 days to review the original IND submission. The process protects volunteers who participate in clinical trials from unreasonable and significant risk in clinical trials. FDA responds to IND applications in one of two ways: approval to begin clinical trials or clinical hold to delay or stop the investigation. FDA can place a clinical hold for specific reasons, including: participants are exposed to unreasonable or significant risk, investigators are not qualified, materials for the volunteer participants[114] are misleading, the IND application does not include enough information about the trial's risks.

A clinical hold is rare; instead, FDA often provides comments intended to improve the quality of a clinical trial. In most cases, if FDA is positive that the trial meets Federal standards, the applicant is allowed to proceed with the proposed study.

9.3. The different phases

The study begins with Phase 1, which lasts several months, and the testing involves both healthy volunteers and people with the disease/condition (20 to 80 people). The purpose of this step is to test safety and dosage: researchers adjust dosing schemes based on animal data (preclinical phase, see *ante*) to determine the percentage of the drug that the human body can tolerate, what its acute side effect are, and generally how it works in humans. The studies also allow an early outline of effectiveness, and how the treatment should

[112] US FDA official site, *Step 2: Preclinical Research,* available at: https://www.fda.gov/ForPatients/Approvals/Drugs /ucm405658.htm (last consulted 08/11/2018).
[113] US FDA official site, *Step 3: Clinical Research*, available at: https://www.fda.gov/ForPatients/Approvals/Drugs/ucm405622.htm (last consulted 08/11/2018).
[114] US FDA official site, *Step 3: Clinical Research,* cit.

best be administered to limit risks and maximize possible benefits.[115] Approximately 70% of the investigated drugs move to phase 2.

Phase 2 involves up to several hundred people with the disease/condition, lasting from several months up to 2 years, to evaluate the drug's efficacy and side effects. These studies aren't large enough to show whether the drug will statistically be beneficial; instead they provide additional safety data, and an additional skimming: only 33% of drugs move to the next phase[116].

Phase 3 (pivotal studies) involves 300 to 3,000 volunteers who have the disease/condition, lasting from 1 to 4 years to demonstrate whether or not the product will be effective. Monitoring the potential adverse reactions, this phase provides most of the safety data as in previous studies it is possible that less common side effects might have gone undetected due to the restricted research pool and amount of time. Approximately 25-30% of drugs move to the last phase[117].

Phase 4, involves several thousands of volunteers, who have the disease/condition, and the trials to test safety and efficacy, are carried out once the drug has already been approved by the FDA, during the Post-Market Safety Monitoring[118].

If a drug developer has evidence from its early tests and preclinical and clinical research that a drug is safe and effective for its intended use, the company can file an application to market the drug, the New Drug Application (NDA). The FDA review team thoroughly examines all submitted data on the drug and makes a decision to approve or not to approve it[119]. If the drug has been shown to be safe and effective for its intended use, after the labeling it is approved for marketing and distributed among the public, while the post-market safety monitoring continues. This articulated process was developed to ensure that the distribution of drugs to the public must stand on adequate proof elements relating to safety and efficiency of the new product[120].

[115] US FDA official site, *Step 3: Clinical Research,* cit.

[116] US FDA official site, *Step 3: Clinical Research,* cit.

[117] US FDA official site, *Step 3: Clinical Research,* cit.

[118] US FDA official site, *Step 3: Clinical Research,cit.*

[119] US FDA official site, *Step 4: FDA Drug Review,* available at: https://www.fda.gov/ForPatients/Approvals/Drugs/ucm405570.htm (last consulted 08/11/2018).

[120] M. TOMASI, *Il Diritto alla salute fra emozione e razionalità. Le Right to Try Laws negli Stati Uniti d'America*, in *Rivista AIC*, 2016, available at: http://www.rivistaaic.it/il-diritto-alla-salute-fra-emozione-e-razionalit-le-right-to-try-laws-negli-stati-uniti-d-america.html (last consulted 08/11/2018).

9.4. Accelerated approval

Considering that the standard procedure might take several years to reach the approval a treatment, US laws have provided patients in medical emergencies with some more readily accessible solutions: one of them is the accelerated approval[121]. Accelerated Approval can be applied to promising therapies that treat a serious or life-threatening condition and provide therapeutic benefit over available therapies. This approach allows for the approval of a drug that demonstrates an effect on a "surrogate endpoint" that is reasonably likely to predict clinical benefit, or on a clinical endpoint that occurs earlier but may not be as robust as the standard endpoint used for approval. This approval pathway is especially useful when the drug is meant to treat a disease whose course is long, and an extended period of time is needed to measure its effect. After the drug enters the market, the drug maker is required to conduct post-marketing clinical trials to verify and describe the drug's benefit. If further trials fail to verify the predicted clinical benefit, FDA may withdraw approval[122].

Since the Accelerated Approval pathway was established in 1992, many drugs that treat life-threatening diseases have successfully been brought to the market this way and have made a significant impact on the disease course. For example, many antiretroviral drugs used to treat HIV/AIDS entered the market via accelerated approval, and subsequently altered the treatment paradigm. A number of targeted cancer-fighting drugs also have come onto the market through this pathway[123].

9.5. The drugs' approval process in the EU

The EU's approval process for drugs follows the same purposes and principles as the US process: «assuring safety and efficacy while providing rapid movement of innovative therapies through the investigative and regulatory processes as quickly as possible»[124]. However, the United States and the European Union approach these challenges in different ways.

Whereas the United States have always relied on a strictly centralized process through only one agency, the Food and Drug Administration (FDA), the European Commission synchronized the regulations of the 28 different countries that form the European Union[125]. Thus, whereas the FDA has the advantages of centralization and common rules, the European Union regulates medical drug and device approvals through

[121] US FDA official site, *Development & Approval Process (Drugs)*, available at: https://www.fda.gov/drugs/developmentapprovalprocess/default.htm (last consulted 08/11/2018)

[122] US FDA official site, *Development & Approval Process (Drugs)*, cit.

[123] US FDA official site, *Development & Approval Process (Drugs)*, cit.

[124] G.A.VAN NORMAN, *Drugs and Devices: Comparison of European and U.S. Approval Processes*, in *Science Direct*, 2016, 399, available at: https://www.sciencedirect.com/science/article/pii/S2452302X16300638 (last consulted 08/11/2018)

[125] G.A.VAN NORMAN, *op. cit.,* 400.

a network of centralized and decentralized agencies, throughout its member states. Many of the processes to approve drugs in the EU are similar to those of the FDA: after submitting an application within one or more states, the drug progresses through sequential studies analogous to those in the US.

Phase 1 trials are conducted on a small number of healthy subjects to clarify pharmacology and dose range; Phase 2 trials comprehend several hundred patients with the targeted condition, to investigate the dose-response relationship; and Phase 3 confirmatory trials include several hundred to several thousand patients to substantiate safety and efficacy.[126] The last part of the procedure is however different: while in the US an NDA is submitted to the FDA, in the EU there are four possible pathways to drugs' approval.

The Centralized process is controlled through the EMA. Every member state of the EU is represented on the EMA Committee for Medicinal Products, which issues a single license valid in all EU member states. This route of approval is mandatory for some classes of drugs, such as treatments for HIV/AIDS, oncology, diabetes, neurodegenerative disorders, autoimmune disease, and viral diseases.[127] The National process consists in the possibility for each EU state to have its own procedures for approving drugs that fall outside of those required to undergo the centralized process.[128] The Mutual recognition process allows drugs approved in one EU state via that state's national process to obtain marketing authorization in another EU member state.[129] Lastly, the Decentralized procedure allows manufacturers to apply for simultaneous approval in more than 1 EU state for products that have not yet been authorized in any EU state and do not fall under the mandatory centralized process[130].

Both systems allow subjects affected by grave and life-threatening disease to enter clinical trials as volunteers, or grant access to unauthorized drugs through compassionate use programs.

9.6. Compassionate use

Another way to ensure faster access to new drugs is the Expanded Access, or compassionate use program, which grants access to drugs that are still in phase 3, sometimes even phase 2, of the clinical trials.

[126] G.A.Van Norman, *op. cit.,* 400.
[127] G.A.Van Norman, *op. cit.,* 400.
[128] G.A.Van Norman, *op. cit,* 401.
[129] G.A.Van Norman, *op. cit.,* 401.
[130] G.A.Van Norman, *op. cit.,* 401.

In the past, earlier clinical trials were the only way to access new drugs under development. However, not every patient meets the enrollment criteria, and participation is difficult for patients with life-threatening, long-lasting or seriously debilitating diseases like rare diseases.

Early access programs like Expanded Access, or the "Compassionate Use Program (CUP)" in the EU, have generated alternative channels for such patients.[131] These programs allow the use of investigational drugs, biological or medical devices outside the clinical trial setting for treatment purposes.

Compassionate use programs in the EU are coordinated and implemented by Member States, which set their own rules and procedures. In the US Expanded access may be granted when the doctor believes that the patient has a serious disease or condition, that might threaten the patient's life, and for which there is no comparable or satisfactory alternative therapy to diagnose, monitor, or treat the disease or condition. Additionally, the patient enrollment in a clinical trial must not be possible, and the potential patient benefit must justify the potential risks of treatment. Moreover, providing the investigational medical product must not interfere with investigational trials that could support a medical product's development or marketing approval for the treatment indication.[132] As for the US program, in 2009 the access granted was expanded, comprehending access to drugs still in phase 1, if the patient is affected by an immediately life-threatening disease. In exceptional cases, the FDA might even grant access to drugs which provide no information on their use on human beings. It is also to be noted that the FDA has approved almost the totality of the requests it has received, the number of which was fairly low[133].

9.7. A critical overview of Right to Try laws

From the analysis of the Extended Access program it is to be inferred that compassionate use provides patients with life-threatening diseases basically equivalent possibilities to the ones provided by the right to try laws. This is the basis of the argumentation made against right to try laws: they provide the patients with a right they substantially already have, while giving them the illusion of having something more.

Several bioethicists and other scholars have questioned the extent to which these laws will actually benefit patients. Jonathan Darrow, Arthur Caplan, Alta Charo, Rebecca Dresser, and others have pointed out that the laws do not require physicians to prescribe these experimental therapies, and also they do not require

[131] G. BALASUBRAMANIAN, S. MORAMPUDI, P. CHHABRA, A. GOWDA, B. ZOMORODI, *An overview of Compassionate Use Programs in the European Union member states,* in *NCBI,* 2016 available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5116859/ (last consulted 02/07/2018).
[132] US FDA official site, *Expanded Access,* available at: https://www.fda.gov/NewsEvents/PublicHealthFocus/ExpandedAccessCompassionateUse/default.htm (last consulted 08/11/2018).
[133] M. TOMASI, *op. cit.,* 15.

insurance companies to pay for them, nor do they require manufacturers to provide them[134] [135]. Because of this, the laws do not actually provide a real right to receive experimental therapies, as the lack of obligations on the other subjects and stakeholders involved makes it nearly impossible to fulfill the "Right to try": these laws should «be considered toothless legislation that offers only false hope to dying people»[136] [137].

Even if the laws work as intended, they would be problematic according to critics. In fact, because the laws require only that drugs have completed only the first of the three phases of clinical testing that take place before the approval, there is no certain data on the efficacy or safety of the drugs, especially in very sick people[138]. In fact, even though phase 1 is the one in which safety and dosage are tested, most of the safety data are actually collected up to phase 3, meaning that administering phase 1 drugs could cause more damage than benefit, and making it impossible to foresee the consequences.

Additionally, efficiency is tested from phase 2 on, meaning that no actual information on efficiency can be given to the patient[139]. This makes informed consent on the part of the patient more difficult to obtain, because informed consent entails by definition: first, knowledge of the pros and cons of a proposed treatment and second, a decision made in light of those pros and cons.[140]Medical and health experts have also voiced concerns, as access to unapproved drugs could hasten death or cause increased suffering in sick patients[141].

Peter Temin wrote that «there is always a chance that any given drug will fail to cure a condition or will induce an adverse reaction», such as developing other conditions, worsen the already present ones or even dying.[142] Drugs that are not fully studied may lead to more adverse reactions in patients, and these laws reduce FDA oversight on drug regulation, that has until now helped avoid such situations[143]. In April 2017, oncologist David Gorski wrote in Science-Based Medicine that the right-to-try laws are harmful to society as they are

[134] B. Dennis, A. Eunjung Cha, *'Right to Try' Laws Spur Debate Over Dying Patients' Access to Experimental Drugs,* in *Washington Post,* 2015.

[135] J. Darrow, *Practical, Legal, and Ethical Issues in Expanded Access to Investigational Drugs*, in *New England Journal of Medicine*, 2015.

[136] A. Bateman-House, A. Caplan, *All Hat, No Cattle—The False Hope of Right to Try Laws*, in *Harvard Health Policy Review*, 2016.

[137] M. Munz, *Missouri's 'Right to Try' Law No Guarantee Patient Will Get Experimental Drugs*, in *St. Louis Post-Dispatch*, 2016.

[138] M. Tomasi, *op. cit.,* 15.

[139] M. Tomasi, *op. cit.*, 16

[140]A. Bateman-House, *Right-to-Try Laws: Hope, Hype, and Unintended Consequences*, in *Annals of Internal Medicine*, 2016.

[141]D. Gorski, *The False Hope of 'Right to Try' Metastasizes to Michigan*, in *Science-Based Medicine*, 2016.

[142] P. Temin, *Taking Your Medicine: Drug Regulation in the United States*, in *Cambridge: Harvard University Press*, 1980.

[143] E. Silverman, *'Right to Try' Laws Wrong to Skirt FDA*, in *Boston Globe,* 2016.

popular with the public who do not understand how the FDA works. Gorski calls this "placebo legislations", as they «make lawmakers feel good, but they do nothing concrete to help actual patients»[144].

Criticisms arose also because the right to try law do not solve the health insurance problems in the US: some states' right-to-try laws also put patients at risk of losing hospice or home health care[145], and the costs surrounding treatment can be prohibitive. The laws mostly attribute the costs of the treatments to the patients, with no burden of payment on health insurances, and with no obligations for the producer to provide the treatment for free. These right to try laws risk to turn the right to health into something accessible only to people who can afford it[146]. Bioethicist Alta Charo called the laws «a simplistic way of going after much more complicated issues»[147]. Initially these laws were also criticized for being unconstitutional, because through them the singular states were regulating medicine, despite the fact that federal legislation has the competence to regulate interstate marketing of medicine[148]. However, considered that a federal right to try law has been recently approved, as mentioned above, it seems that this argument is no longer valid.

9.8. Common criticalities

The first argument against self-experimentation that could be drawn from the enactment of right to try laws, is the necessity of the overcoming of Phase 1 of the approval process. This requirement provides the patient and the doctors with basic safety and dosage data that, even if arguably enough to eliminate all risks, at least give the subject more consciousness. This awareness cannot be found in the practice of self-experimenting with an entirely untested drug, which often has not undergone even preclinical trials, being developed outside the institutionalized process.

A second argument revolves around the critics concerning safety and efficiency of treatments that have undergone only Phase 1 of the approval process. It is claimed, as outlined above, that the safety and dosage data collected in the first phase are just a small amount of the entirety of data that are collected throughout the entire process, up until phase 3. This implies that the research concerning an outright untested drug provides absolutely no data on the toxicity of the treatment. The same holds true for efficiency, tested in phase 2, implying that not only the drug could harm the patient, but even if it did not, it is not likely to have beneficial results either.

---

144 D. GORSKI, *op. cit.*

145 L. KEARNS, A. CAPLAN, *Right-to-Try Legislation Punishing*, in *Albany Times Union*, 2016.

146 M. TOMASI, *op. cit.,* 16.

147 K. LEONARD, *Seeking the Right to Try*, in *U.S. News & World Report*, 2015.

148 T. YANG, *'Right to Try' Legislation: Progress or Peril?*, in *Journal of Clinical Oncology,* 2016.

On the contrary, it is highly probable that the self-experiment could result in death, or increased suffering for the sick patient due to adverse reaction that could not be foreseen due to the lack of data. On these grounds, due to the absence of these data that can only be provided by clinical trials, the given consent that can be considered as implied when speaking about self-experimentation, might not be entirely informed and therefore valid consent. As many experts, as discussed above, regard the consent given with the information gathered in phase 1 of the clinical trials as not to be entirely informed consent, this is to be transposed to self-experimentation as well. In fact, it cannot be considered informed, as it is given without the basic information that at least one phase on clinical trial would give.

A third argument might revolve around the total absence of FDA oversight on the practice: as right to try laws reduce this control, it is entirely erased when self-experimentation comes into consideration. This undermines the scientific validity of the results of the experiment, as explained before.

Another element threatening legitimacy of the experiment is the statistical value of one-subject testing: the fact that phase 1 alone involves testing on 20 to 80 subjects speaks for itself, even without taking into consideration that the entire process of approval involves several hundreds of subjects.

In view of this, it is to be noted that, although right to try laws and self-experimentation are two different phenomena, they share some critical issues, mostly concerning reliability and the health of the patient.

10. Conclusions

In light of the above, it can be inferred that self-experimentation is a difficult concept both to condemn — because of its history of fast forwarding medical knowledge — and to endorse — due to the high risks and, as some would say, the lack of rigour and self-serving nature of a solo experiment[149].

As for the current situation, it appears that only a scarce legal framework, mainly deriving from human experimentation regulation is present, despite the ever-increasing presence and alarming normalization of self-experimentation in the research field.

This absence of specific legislation and procedures or protocols to be followed, endows researchers, but also biohackers and “common people”, with a freedom of choice that is not always balanced by the necessary knowledge: nothing is preventing them to choose self-experimentation over regulated clinical trials to

[149] R. GHANI, *op. cit.,* 1.

"legitimize" a certain research, theory or treatment. This might endanger them, but it might also affect the public's perception of the practice, leading to the assumption that the potentially positive results obtained, make the treatment injected safe enough to be used by anyone who might need it.

Furthermore, when the experiment is led by inexperienced people (i.e. Tristan Roberts), the public might assume that anyone could perform self-experimentation and "get away with it". This could not be further from the reality of research and experimentation, if the number of deaths resulting from it are of any indication (see *Table I*). Up to this point, no lay person has been harmed through the means of self-experimentation, but as the practice is rapidly and largely spreading these data might change.

Against this background, the argument of self-determination on its own is not enough to uphold the practice of self-experimentation performed by physicians or researchers, and most certainly not by amateurs.

While we might have rights on our own body, these rights are limited by common sense, but also by the law. An example is the widely spread opinion that, even if the Italian Constitution grants the right to refuse non mandatory treatments, that does not automatically grant people the possibility to use on themselves every other kind of experimental treatment they might want.[150] This might also be said for any compassionate use of untested treatments, and therefore also for Right to Try laws, and self-experimentation.

Limitations to the principle of self-determination might also be found, for instance, taking into consideration Article 5 of the Italian Civil Code. From the latter it stems that any act of disposition of one's own body is prohibited when it might cause a permanent diminishment of physical integrity, or when it is contrary to national and international law, public order or common decency.

Furthermore, even though we have certain rights on our body, we need to take into consideration the effects of our actions on other people, against whom we have obligations and responsibilities. For instance, physicians have a responsibility towards their patients, that might be breached if the self-experiment performed might lead them to confide in a treatment or a diagnosis that has no other scientific support and lacks the kind of legitimization that only an institutionalized process can grant.

In light of the above, it is safe to say that an ethical and legal framework of the practice of self-experimentation is significantly needed, as the practice is rapidly spreading and evolving, escaping any already present legislation that might be applied analogically.

A proposal for a legislation concerning self-experimentation might revolve around the principle of transparency, and the need for a standardized procedure, including the approval of an ethics committee,

[150] Comitato Nazionale per la Bioetica, *Cura del caso singolo e trattamenti non validati*, downloaded Pdf from http://www.biodiritto.org/ (last consulted 08/11/2018).

created purposely for the evaluation of self-experiments. The procedure could resemble the one laid down by the FDA for the Development & approval process for drugs, comprising a set of steps ensuring at least the absence of toxicity and the dosage of the treatment to be injected, as it is done in Phase 1 of the clinical trials.

Nevertheless, the control of the ethics committees shall be based on standards and provisions specifically intended to regulate self-experimentation, and not human experimentation in general. This necessity is linked to the aforementioned problem: ethical commissions would mainly not approve self-experimentation, if the evaluation was based on human experimentation regulations, which are not tailored to the specific characteristics of this different practice. Instead, specifically developed standards might lead to the approval of safer research involving self-experiments, avoiding the need for the subjects to act outside the institutionalized procedure and settle for an *a posteriori* recognition (see *above*).

Furthermore, the enactment of measures to prevent plagiarism, might convince even the more reluctant researchers to participate in the institutionalized procedure.

On the same grounds, the legislation shall impose a set of standards to be met by the experiment in order to gain the approval: i.e. the experiment must not result in death, to the best of the experimenter's knowledge. Also, a definite level of toxicity might be set, under which experiments of new treatments are allowed; or certain results need to be achieved in the preclinical trials, to enable experimentation of any kind on humans.

As stated previously, the entire legislation, and consequently the procedure developed, should be focused on a principle of transparency: this would ensure a higher level of safety for the self-experimenter, but also for the public. As a matter of a fact, transparency on the development of the research, and on the purpose of the experiment would increase the information accessible to the experimenter himself, if he's not the developer, and the public who might want to participate in the following experimentation. Furthermore, full disclosure on the content of the research and the aim of the experiment might allow ethics committee to perform more meaningful controls.

Lastly, self-experimentation should be limited strictly to professionals: every individual who is not trained in medical-related fields must not be allowed to experiment on him/herself. This prohibition shall be based on the afore analyzed idea that the right to self-determination is not enough to support uncontrolled self-experimentation performed by non professionals, if public interest to safety comes into consideration.

As mentioned above, on the one hand, these experiments might persuade the public that a certain treatment is safe enough to be used by anybody, if the results are positive; on the other hand, it might have dangerous

results for the person performing it, or might also spread diseases to other people. Hence, the need to at least restrict this practice, as it is not likely to be completely erased, to a controlled and institutionalized area.

In order to actualize this prohibition, related provisions and bans on the sale of these untested treatments on the market shall be enacted. These bans must forbid companies like Ascendance and ODIN the sale of unapproved treatments, even if, as they claim, «they need some steps to effectively work, ensuring that the buyer has at least some kind of scientific knowledge» (see *above*). More so, they must prohibit the sale, when it is done purely for «research purpose», as Traywick has argued (see *above*), as research must be conducted according to the new set of rules and standards that shall be enacted.

The offense shall be qualified as a felony, given the fact that it is potentially dangerous to a wide public, and it is contrary to the public order and safety, and should therefore entail prison sentences greater than a year.

The prohibitions shall also cover the purchase of these treatments, if not as far as to entail a felony, at least qualifying such purchase as an infraction, which shall trigger a fine, and if repeated a misdemeanor, which can lead to up to a year in jail time.

This set of standards, guidelines and prohibitions should set a definite legal framework on self-experimentation, regulating this practice that seems unlikely to be erased entirely just by a general ban, as such a prohibition might possibly cause the creation of a black market of untested drugs. Instead, the allowance of the practice, although under a strict set of defined requirements and restrictions, might avoid such an outcome, and on the contrary provide the patients and the researchers with sufficient protection.

In such a manner, international law would ensure an overall safer research environment both for professionals and subjects of the experiments, even if they are indeed the same person.