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IMMORALITY OF HUMAN EXPERIMENTATION IN DEVELOPING COUNTRIES AND INTERNATIONAL CRIMINAL LAW: A CRITICAL MEDICO-LEGAL ASPECTS

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Abstract

Since Nuremberg, the ethics of scientific research involving human beings has been for decades the source of concern and controversy. Profit-driven experimentation sponsored by the pharmaceutical industry has progressively migrated to the South, turning into a widespread phenomenon imbued with ethical challenges and dilem- mas. The protection of vulnerable communities from the risks of unethical behaviour and exploitation, often associated with the outsourcing of clinical trials in developing countries, calls for respect of internationally agreed standards. This Article argues that massive experiments conducted in disregard of universal bioethical principles and hu- man rights may amount to crimes against humanity under international criminal law. It also suggests that, in such cases, the International Criminal Court would have juris- diction over a broad range of liable individuals, including public officials of host and sponsoring States, physicians and researchers acting in their private capacity, as well as officers and directors of pharmaceutical corporations.

Keywords

clinical trials – ethics of medical research – unlawful human experimentation – international criminal law – war crime – crime against humanity – accountability of pharmaceutical corporations – State responsibility

1. The Business of Clinical Research in the Global South:

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Profit versus Ethics

Pharmaceutical and medical research can make a crucial contribution to glob- al public health, but it can also turn into unscrupulous business, abuse and crime.[1] The ethics of experimentation involving human beings,[2] which has been for decades the source of concern and controversy after the Nazi experience, is still the object of lively debate due to the emergence of new forms of human exploitation and medical misconduct. Unethical and harmful experimentation performed on vulnerable populations in developing countries is a dramatic case in point.

It is reported that more than half of all drug trials worldwide take place in developing or newly industrialised countries. The globalisation of human experimentation is the result of two major driving forces: first, a growing need for clinical trials[3] generated by the increased medicalisation of Western societies and the rising demand for newer and better treatments and drugs;[4] second, a profit-driven approach to medical research, which is replacing medical ethics with business ethics.

In this latter respect, it has to be noted that the management and conduct of clinical trials has progressively moved from State-controlled and publicly- funded institutions and research centres to the pharmaceutical industry and other private actors, like contract research organisations (CROs).[5] In addition to this, several academic institutions and governmental agencies are

[1] M. Cherif Bassiouni observed: '[b]ecause human experimentation deals with effects upon large numbers of people, experimenters possess the potential to enhance or dimin- ish the welfare of mankind. Since this potential may result in wilful, reckless or inadver- tent acts harmful to human beings, human experimentation is also a proper concern for the international criminologist'. *See* 'The Crime of Human Experimentation', in M. Cherif Bassiouni (ed.), *International Criminal Law: Crimes* (Transnational Publishers, Ardsley, 1986), pp. 399–421, p. 399.

[2] There are two major kinds of human experimentation: 'therapeutic experimentation', which implies treating a sick person with new methods and drugs for purely therapeutic purposes, and 'research experimentation', which treats individuals with new methods and drugs for purely scientific or testing purposes.

[3] Clinical trials are part of the extensive testing process undergone by new drugs in order to ob- tain approval by regulatory authorities. This process begins with laboratory studies followed by testing on animals. If this proves promising, four phases of clinical research follow. Phase one is usually conducted on a relatively small number of healthy volunteers, who are often paid for their participation, and is intended to determine what dosage of the drug is required to produce a response in the human body, how the body processes the drug, and whether the drug produces toxic or harmful effects. Phase two is conducted on a group of patients who have the disease that the drug is intended to treat. Its goals are to determine whether the drug has any beneficial effect on the disease and has any harmful side effects. Phase three is the clinical trial, in which the drug is administered to a large number of patients and com- pared to another drug, if there is one for the condition in question, and/or to a placebo. Phase four takes place after the drug is licensed and marketed and it consists in the monitoring of possible side effects that did not show up in the earlier phases (post-marketing surveillance or pharmacovigilance).

[4] *See* Paddy Rawlinson, 'Ethics v. Economics: The Cost of Outsourcing Clinical Trials to Devel- oping Countries', available at http://scitechconnect.elsevier.com/clinical-trials-developing-countries/.

[5] CROs provide support to the pharmaceutical, biotechnology, and medical device industry in the form of research services outsourced on a contract basis. Their services include bio- pharmaceutical development, biologic assay development, commercialisation, preclinical research, clinical research, clinical trials management, and pharmacovigilance.

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increasingly dependent upon major corporate money, so that the entire field of medical research is permeated by conflicts of interest. Such a change in paradigm has inevitably caused a shift in the drivers and objectives of medical research – which is said to respond to the market rather than to moral or beneficent concerns[6]– and has paved the way for human experimentation to progressively migrate to the global South. In low-income countries, clinical trials have in fact proved to be easier, cheaper and faster. The research business has taken advantage of lax regulations and corruption, while high levels of poverty and illiteracy have made it possible to enrol everlarger numbers of 'volunteers'.[7] The outsourcing of clinical trials in the developing world has thus turned into a widespread practice imbued with ethical and legal challenges.[8]

The concerns raised by this phenomenon have become ever more compel- ling after the public unveiling of massive experiments performed in disregard of internationally agreed principles of medical ethics and basic human rights.[9]

In such a scenario, the most appalling cases that have come to light concern the testing of vaccines and drugs on children. These experimentations, sponsored by Western pharmaceutical companies, have also involved governmental agencies and public health institutions. Among the most notorious examples are Pfizer's tests of an experimental antibiotic against meningitis in Nigeria,[10]

[6] In her work on the social organisation of the 'global experimental enterprise', Adriana Pet- ryna states that 'pharmaceuticals are the new gold': *When Experiments Travel: Clinical Trials and the Global Search for Human Subjects* (Princeton University Press, Princeton, 2009), p. 11.

[7] Rawlinson, *supra* note 4; *see also* Paddy Rawlinson and Vijay K. Yadavendu, 'Foreign Bodies: The New Victims of Unethical Experimentation', 54 *The Howard Journal of Criminal Justice* (2015) 8–24, pp. 9–10.

[8] *See* Seth W. Glickman, John G. McHutchison, Eric D. Peterson, Charles B. Cairns, Robert A. Harrington, M. Califf and Kevin A. Schulman, 'Ethical and Scientific Implications of the Globalization of Clinical Research', 360 *New England Journal of Medicine* (2009) 816–823.

[9] Marcia Angell, 'The Ethics of Clinical Research in the Third World', 337 *The New England Journal of Medicine* (1997) 847–849; Zulfiqar Ahmed Bhutta, 'Ethics in International Health Research: A Perspective from the Developing World', 80 *Bulletin of the World Health Organization* (2002) 114–120; Joanne Roman, 'U.S. Medical Research in the Developing World: Ignoring Nuremberg', 11 *Cornell Journal of Law and Public Policy* (2002) 441–460; Ezekiel J. Emanuel, David Wendler, Jack Killen and Christine Grady, 'What Makes Clini- cal Research in Developing Countries Ethical? The Benchmarks of Ethical Research', 189 *The Journal of Infectious Diseases* (2004) 930–937; Colleen C. Denny and Christine Grady, 'Clinical Research with Economically Disadvantaged Populations', 33 *Journal of Medical Ethics* (2007) 382–385; Cláudio Lorenzo, Volnei Garrafa, Jan Helge Solbakk and Susana Vidal, 'Hidden Risks Associated with Clinical Trials in Developing Countries', 36 *Journal of Medical Ethics* (2010) 111–115; Ilja Richard Pavone, 'Medical Research in Developing Coun- tries and Human Rights', in Jan Schildmann, Verena Sandow, Oliver Rauprich, and Jochen Vollmann (eds.), *Human Medical Research* (Springer, Basel, 2012), pp. 65–87; Remigius N. Nwabueze, *Legal and Ethical Regulation of Biomedical Research in Developing Countries* (Routledge, Abingdon, 2013).

[10] These trials took place during Africa's worst ever meningitis epidemic in 1996. They were performed on 200 children without obtaining the parents' proper informed consent. Throughout the experimentation eleven children died and others were blinded, paralysed or brain-damaged. Their relatives and the Nigerian government sued Pfizer and in 2009 a settlement was achieved between the company and the Nigerian government. In 2011, after a 15-year long legal battle against the company, four families received compensation for the death of their children. *See* David M. Carr, 'Pfizer's Epidemic: A Need for Interna- tional Regulation of Human Experimentation in Developing Countries', 35 *Case Western Reserve Journal of International Law* (2003) 15–53; Emmanuel R. Ezeome and Christian Simon, 'Ethical

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the covert clinical trial of an experimental measles vaccine performed by the U.S. Center for Disease Control with the co-sponsorship of Kaiser Permanente,[11] and the trials of an experimental rotavirus vaccine conducted in India on thousands of children.[12] Many more examples of unethical clinical research on vulnerable subjects could be offered, including, first and foremost, trials on pregnant and breast-feeding women in Asia and Africa to test antiretroviral drugs for the prevention of mother-child transmission of HIV.[13]

Against this backdrop, this paper examines the major concerns raised by the globalisation of clinical trials in the light of generally accepted principles of research ethics building on the Nuremberg legacy, as well as of the relevant international biolegal framework. It also explores the different regimes of accountability of States and non-state actors for clinical research which is not only unethical, but also unlawful under international human rights law and international criminal law. The paper suggests that massive unethical trials, performed under particularly inhumane and harmful conditions, may amount to crimes against humanity triggering the jurisdiction of the International Criminal Court (icc) over a broad range of liable individuals.

2. The Nuremberg Legacy: International Ethical Standards for Human Experimentation

The reaction of the international community to the scourge of human experimentations carried out during World War II STARTed a new wave of reflections on medical ethics and the limits to be imposed on researchers and physicians. The infamous Nuremberg Doctors' Trial, known as the *Medical*

Problems in Conducting Research in Acute Epidemics: The Pfizer Menin- gitis Study in Nigeria as an Illustration', 10 *Developing World Bioethics* (2008) 1–10.

[11] In 1990 more than 1.500 six-month old Black and Hispanic babies were inoculated with an experimental measles vaccine without informing their parents that the vaccine was experimental. This vaccine had been tested already in Mexico, Gambia, Guinea, Togo, Senegal, Haiti in the 1980s, resulting in high death rates and an increased risk of autism. CDC SCIENTISTS intentionally concealed evidence of these risks for more than 10 years. *See* at http://ahrp.ORG/1990-fda-issued-a-waiver-from-informed-consent-cdc-covertly-tested- experimental-vaccine-on-black-latino-babies/.

[12] These clinical trials took place on 6.800 children between 2011 and 2012 and were fund- ed by multiple private and government sources, including the Bill & Melinda Gates Foundation and the National Institutes of Health. More than 2.000 children received placebo injections of salt water. Given the availability of two highly effective rotavirus vaccines at the time the study was initiated – RotaTeq, marketed by Merck & Co., and Rotarix, marketed by GlaxoSmithKline – the failure to provide infants with one of these two vaccines instead of a placebo violated international ethical standards for conducting human research. *See* at http://www.huffingtonpost.com/michael-carome-md/unethical -CLINICAL-TRIALS_B_5927660.html.

[13] *See* Peter Lurie and Sidney M. Wolf, 'Unethical Trials of Intervention to Reduce Perinatal Transmission of the Human Immunodeficiency Virus in Developing Countries', 337 *The New England Journal of Medicine* (1997) 853–856; Georges J. Annas, 'Human Rights and Maternal-Fetal HIV Transmission Prevention Trials in Africa', 88 *The American Journal of Public Health* (1998) 560–563.

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case,[14] revealed that hundreds of thousands of prisoners of war and detainees in Nazi concentration camps were subjected to all kind of inhuman medical procedures (including tests on the effects of high altitude and low pressure, freezing experiments, seawater experiments, poison experiments, incendiary-bomb experiments, infections, forced sterilisation, muscle/nerve/bone regeneration and bone transplantation). Evidence was also produced that Chinese, Korean and Russian prisoners of war were similarly used as subjects for medical research by the Imperial Japanese Army, which infected them with various highly dangerous pathogens (including plague, cholera, epidemic haemorrhagic fever, tuberculosis, typhoid, tetanus, and anthrax) and also used them for vivisections and demonstrations of surgery techniques.

As is well known, these heinous practices prompted the drafting of the Nuremberg Code, a set of ten principles stating the standards to be applied to medical experimentation in order to satisfy moral, ethical and legal requirements. In establishing the primacy of the human being over any other interest of science – and hence the imperative for scientists and physicians to respect the will of the subjects involved in experimentation and the duty to protect their safety and health – the *Medical* case judgment and the Nuremberg Code laid the foundations for embedding the 'scientific legality' of medical practice at the intersection of criminal law and deontological rules.[15] In this sense, the Nuremberg principles marked a watershed between cruel and unregulated experiments and the affirmation of the ethics of medical research.[16]

Despite the fact that the Nuremberg language was attacked under many re- spects, the very essence of the Code was endorsed by the World Medical As- sociation, first in its Principles for Those in Research and Experimentation of 1954 and then in the famous Declaration of Helsinki (DoH).[17]

The goal of the Declaration was precisely to elaborate a body of deonto- logical rules, conceived

[14] Nuremberg Tribunal, *United States of America* v. *Karl Brandt and others*, Judgment of 20 August 1947.
[15] Xavier Aurey, 'Le droit international pénal de la bioéthique', in Hervé Ascensio, Emmanuel Decaux, and Alain Pellet, *Droit international pénal* (Pedone, Paris, 2012), pp. 261–276, p. 262.
[16] The Nuremberg principles can be summarised as follows: voluntary and informed con- sent is essential; the research subject should be free to stop the experiment at any time; the experiment should produce valuable benefits for the society; the experiment should be based on animal experimentation and anticipated results should justify its perfor- mance; the conduct of the research should avoid all unnecessary physical and mental suffering and injury; the degree of risk should never exceed that related to the nature of the problem; the experiment should be conducted by a qualified team of researchers in appropriate facilities that protect research subjects from harm or death; the experiment should be promptly stopped if its continuation is likely to result in injury, disability, or death.
[17] WMA, Declaration of Helsinki – Ethical Principles for Medical Research Involving Human Subjects, 1964 (revised in 1975, 1983, 1989, 1996, 2000, 2008 and 2013)

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by physicians for physicians, and aimed at preventing misconduct in biomedical research and human rights violations. In its original version, the DoH made a distinction between essentially therapeutic clinical research and pure clinical research and thus adopted different guidelines (Medical Research Combined with Professional Care and Non-Therapeutic Medical Research) in addition to twelve common basic principles concerning biomedical research involving human subjects. In its latest version (2013), the text of the Declaration combines the enunciation of fifteen general principles with a remarkable number of additional precepts focusing on: risks, burdens and benefits; vulnerable groups and individuals; scientific requirements and research protocols; research ethics committees; privacy and confidentiality; in- formed consent; use of placebo; post-trial provisions; research registration and dissemination of results; unproven interventions in clinical practice.

Both the Nuremberg Code and the DoH have influenced the formulation of international, regional and national regulation. Among the international soft law instruments that have followed, noteworthy are the International Ethical Guidelines for Biomedical Research Involving Human Subjects ad- opted by the Council for International Organizations of Medical Sciences in 1982 (revised 1993 and 2002), the WHO Guidelines for Good Clinical Practice for Trials on Pharmaceutical Products (1995), the Guideline for Good Clinical Practice drafted by the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (1996), the UNAIDS Guidance Document on Ethical Considerations in HIV Preventive Vaccine Research (2000), and the UNESCO Universal Declaration on Bioethics and Human Rights (2005). In the realm of hard law, especially European law, the principles enshrined in the DoH were incorporated in the Council of Europe Convention on Biomedicine and Human Rights[18] and its Additional Protocol on Biomedical Research,[19] as well as in the EC Clinical Trials Directive 2001/20,[20] recently replaced by the EU Clinical Trial Regulation No. 536/2014.[21]

Gathering the legacy of the Nuremberg Code, the core principles embodied in all these instruments

[18] Convention for the Protection of Human Rights and Dignity of the Human Being with regard to the Application of Biology and Medicine: Convention on Human Rights and Biomedicine, CETS No. 164, Oviedo, 4 April 1997 ('Oviedo Convention').
[19] Additional Protocol to the Convention on Human Rights and Biomedicine, concerning Biomedical Research, CETS No. 195, Strasbourg, 25 January 2005.
[20] Directive 2001/20/EC of the European Parliament and of the Council of 4 April 2001 on the approximation of the laws, regulations and administrative provisions of the Member States relating to the implementation of good clinical practice in the conduct of clinical trials on medicinal products for human use, *OJ* L 121, 1 May 2001, p. 34.
[21] Regulation (EU) No. 536/2014 of the European Parliament and of the Council of 16 April 2014 on clinical trials on medicinal products for human use, and repealing Directive 2001/20/EC, *OJ* L 158, 27 May 2014, p. 1 (applicable as from 28 May 2016).

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point to the primacy of the human being,[22] to respect for his dignity, autonomy and integrity, and to compliance with the ethical principles of beneficence and non-maleficence.

They prescribe that:

a) every proposal/project for medical research on human subjects must be approved by a competent body after independent examination of its sci- entific merit and review of its ethical acceptability;[23]

b) research on humans is possible only if there is no alternative of compa- rable effectiveness;[24]

c) the research must be justifiable on scientific grounds, which means that there must be the prospect of discovering new ways of benefiting peo- ple's health and an expectation that important scientific knowledge will be the result;[25]

d) the populations in which the research is carried out should benefit from the results of the research (social value and benefit-sharing);[26]

e) risks to the research subjects (i.e. the potential for an adverse/harmful outcome) must not be unreasonable or disproportionate as compared to the expected benefits of the research; direct and indirect benefits to patients and research participants should be maximised and any pos- sible harm minimised;[27] injured subjects are entitled to treatment and compensation;[28]

f) research should only be carried out with the prior, free, express and in- formed consent of the person concerned, who can withdraw it at any time; exceptions must comply with ethical and legal standards; research subjects who are unable to give consent (children, severely mentally impaired individuals, unconscious patients) can still serve as research subjects but only for their direct health benefit and under restricted conditions;[29]

g) research subjects have a right to privacy with regard to their personal health information;[30]

[22] DoH, para. 8; Oviedo Convention, Art. 2; Additional Protocol, Art. 3; Regulation 536/2014, Art. 3.
[23] DoH, para. 23; CIOMS Guideline 2; Oviedo Convention, Art. 16 (iii); Additional Protocol, arts. 7, 9; UNESCO Declaration, Art. 19; Regulation 536/2014, Art. 4.
[24] Oviedo Convention, Art. 16 (i); Additional Protocol, Art. 5.
[25] DoH, para. 21; CIOMS Guideline 1; Additional Protocol, Art. 8.
[26] DoH, paras. 16, 20; CIOMS Guidelines 10, 12; UNESCO Declaration, Art. 15.
[27] DoH, paras. 16–18; CIOMS Guidelines 8–9; Oviedo Convention, Art. 16 (ii); Additional Pro- tocol, arts. 6, 17 and 21; UNESCO Declaration, Art. 4; Regulation 536/2014, Art. 28.
[28] DoH, para. 15; CIOMS Guidelines 19, 21; Additional Protocol, Art. 31; Regulation 536/2014, Art. 76.
[29] DoH, paras. 19–20, 25–32; CIOMS Guidelines 4–6, 13–17; Oviedo Convention, arts. 16 (iv-v), 17; Additional Protocol, arts. 13–16; UNESCO Declaration, arts. 6 (2), 7 (b); Regulation 536/2014, Arts. 28–33
[30] DoH, para. 24; CIOMS Guideline 18; Additional Protocol, arts. 25–26; UNESCO Declara- tion, Art. 9.

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h) to guarantee the integrity of the research, researchers should solve pos- sible conflicts of roles and interest; they should refuse to participate in unethical research.[31]

Despite their recognised universal value and scope, the application of these principles has proved to be particularly critical in the context of clinical re- search in developing countries, where some of these basic precepts are often disregarded.

3. Ethical Issues Concerning Clinical Research in Developing Countries

As said before, the outsourcing of clinical research in the global South has be- come a widespread phenomenon raising serious ethical and legal concerns. Indeed, the conduct of clinical trials by Western governments and pharmaceu- tical companies has often brought forth charges of unethical behaviour and exploitation, while the existing divide between the ethics and the reality of medical research has stimulated a profound discussion on the 'geographic mo- rality' of research.[32]

To shield large communities from the risks associated with human ex- perimentation, it is firmly asserted that local authorities should always keep control on the ethics and legality of externally sponsored research,[33] and that they should also be capable of imposing regulations that prevent abuses and human rights violations. As aptly noted, guaranteeing the primacy of human beings and public interests over the private interests of sponsoring countries or corporations is key to minimising risks and maximising obtainable benefits (in terms of enhancement of local research capacities, improvement of health facilities and equipment, provision of medicines and health care).[34]

In practice, the major concern in transnational research settings is the vul- nerability of participants and the need to protect their health and safety.[35] In this respect, the most debated

[31] DoH (as revised in 2000), Art. 30; CIOMS Guidelines 10, 12, 20–21; UNESCO Declaration, Art. 15. *See* John R. Williams, *WMA Medical Ethics Manual* (3rd ed., 2015), Chapter 5, espe- cially pp. 103–104, 110–112.

[32] David P. Fidler, '"Geographical Morality" Revisited: International Relations, Internation- al Law, and the Controversy over Placebo-Controlled HIV Clinical Trials in Developing Countries', 42 *Harvard International Law Journal* (2001) 299–354.

[33] *See* commentary to CIOMS Guideline 3: '*externally sponsored research'* refers to research undertaken in a host country but sponsored, financed, and sometimes wholly or partly carried out by an external international or national organization or pharmaceutical com- pany with the collaboration or agreement of the appropriate authorities, institutions and personnel of the host country'.

[34] Lorenzo et al., *supra* note 9, p. 111.

[35] On vulnerability in the legal and ethical discourse, see Roberto Andorno, 'Is Vulnerabil- ity the Foundation of Human Rights?', in Aniceto Masferrer and Emilio García Sánchez (eds.), *Human Dignity of the Vulnerable in the Age of Rights* (Springer, Dordrecht, 2016) pp. 257–272. For an in-depth discussion of the concept of vulnerability (decisional, health- related, etc.) of research participants, *see* Éloïse Gennet, Roberto Andorno and Bernice Elger, 'Does the new

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issues are the medical and social relevance of the research, the quality of informed consent, the standard of care, and the post-trial availability of the tested drugs.[36] Concerns related to respect for the bedrock principle of informed consent include risks of undue inducement through compensation, therapeutic misconception and the role of community consent.[37] Discussion on the application of a 'double standard of care' refers to the controversial use of placebo in control groups and the duty of research- ers to offer the best available therapeutic care, whatever the actual standards in the host country. In relation to this issue, it is contended that accepting the use of placebo in low-income or poor countries, despite the fact that a proven treatment for the studied disease already exists, means allowing an unethical discriminatory standard which dilutes internationally agreed guidelines for purely utilitarian purposes.[38] A third reason of concern is the risk of exploitation in contrast to the required medical and social relevance of the research for the local population[39] and the principle of benefit sharing, which both under- pin the ethical justification of research in third countries. In this respect, it is contended that unless the sponsoring country or corporation makes the drug available to the community on which it was tested, the research amounts to unethical exploitation.[40]

To address these concerns, resort is to be made to the systematic framework of principles and guidelines enshrined in the international instruments mentioned above, which are undoubtedly meant to serve as a common reference also for delocalised clinical trials. Their intended universal

EU Regulation on clinical trials adequately protect vulnerable re- search participants?', 119 *Health Policy* (2015) 925–931, especially at p. 926. On the concept of 'social vulnerability' and the relevant risk-minimisation procedures, *see* Lorenzo et al., *supra* note 9.

[36] Emanuel et al., *supra* note 9, suggested eight core principles and corresponding bench- marks to ethically justify research in developing countries and to guarantee its integrity: collaborative partnership, social value, scientific validity, fair selection of study popula- tion, favourable risk-benefit ratio, independent review, informed consent, and respect for recruited participants and study communities.

[37] *See* Ezekiel J. Emanuel, Xolani E. Currie, and Allen Herman, 'Undue Inducement in Clini- cal Research in Developing Countries: Is It a Worry?', 366 *The Lancet* (2005) 336–340; An- nas, *supra* note 13 (questioning whether this principle can be applied to impoverished populations in developing countries, since everyone in need of care would volunteer for research, being convinced that trials will represent medical treatment); Fidler, *supra* note 32, p. 339 (arguing that cutting the individual out of the consent procedure, in case of community or tribal consent, is not acceptable under international human rights law). *See also* Article 6 (3) of the UNESCO Declaration: '[i]n appropriate cases of research car- ried out on a group of persons or a community, additional agreement of the legal rep- resentatives of the group or community concerned may be sought. In no case should a collective community agreement or the consent of a community leader or other author- ity substitute for an individual's informed consent'.

[38] *See* Annas, *supra* note 13; Lurie and Wolf, *supra* note 13.

[39] DoH, para. 20; Unesco Declaration, Art. 15. *See also* UNESCO, *Report of the IBC on the Prin- ciple of the Sharing of Benefits*, 2 October 2015.

[40] *See* Alice K. Page, 'Prior Agreements in International Clinical Trials: Ensuring the Benefits of Research to Developing Countries', 3 *Yale Journal of Health Policy, Law, and Ethics* (2003) 35–66; Ruth Macklin, *Double Standards in Medical Research in Developing Countries* (CUP, Cambridge, 2004); Kristen Farrell, 'Human Experimentation in Developing Countries: Im- proving International Practices by Identifying Vulnerable Populations and Allocating Fair Benefits', 9 *Journal of Health Care Law & Policy* (2006) 136–161.

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scope is confirmed in several provisions. A relevant example is offered by CIOMS Guideline 3, dedicated to externally sponsored research, which provides that ethical standards applied in a third country should be no less stringent than they would be for research carried out in the sponsoring country. *Ad adiuvandum*, this Guideline also requires that the authorities of the host country, as well as a national or local ethical review committee, should ensure that the research is responsive to the health needs and priorities of the host country and meets the requisite ethical standards. In the same vein, Article 29 of the Additional Protocol to the Oviedo Convention, dealing with research conducted in countries that are not Parties to the Protocol, requires that sponsors or researchers within the jurisdiction of a Party, who plan to undertake or direct a research project in a third State, should ensure that the research project complies with the rules prescribed by the Protocol. Even more articulated is Article 21 of the Universal Declaration on Bioethics and Human Rights, which sets specific ethical standards for 'transnational practices'. This provision states that all public and private subjects associated with transnational research should endeavour to ensure that any activity which is undertaken, funded or otherwise pursued in third States is consistent with the principles set out in the Declaration itself (para. 1); that externally funded research should be the object of an appropriate level of ethical review in the host State and the State in which the funder is located, based on ethical and legal standards consistent with the above-said principles (para. 2); that transnational health research should be responsive to the needs of host States (para. 3); that research agreement concluded be- tween sponsoring and host States should include an agreement on the benefits of research based on equal participation of all parties involved (para. 4). At the European level, too, it is required that clinical trials conducted outside the European Union, in relation to which an application dossier is submitted for marketing authorisation in the EU in accordance with Regulation 536/2014, should be conducted in conformity with principles equivalent to those of the Regulation as regards the rights and safety of the subject.

These provisions, in line with the preambular statement of the UNESCO Declaration that 'all human beings, without distinction, should benefit from the same high ethical standards in medicine and life science research', have paved the way for a strong and widely shared advocacy of universal ethical standards based on non-discrimination.

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4. Accountability of States and Non-State Actors for Unethical Clinical Research Involving Human Rights Violations

Accountability of Pharmaceutical Corporations

Very often the governments of developing states adopt lax policies towards multinational corporations in order to attract foreign investments in the health sector, thus creating what is generally defined a 'conducive environment for clinical trials'. Some of these governments have neither the interest nor the resources to monitor corporate behaviour, which may even lead them to assist companies in human rights violations or grant corporations *de facto* control over territories and populations.[41]

Although no specific regime of international responsibility has been so far designed for multinational corporations, they are not completely *legibus solu- tae*, and a growing trend towards the affirmation of their accountability also at the international level (since it normally operates only at domestic law level) has been progressively reported in international law and practice.[42]

Ever since the MID-1970s, soft law guidelines have been adopted by UN bod- ies and by the Organisation for Economic Cooperation and Development.[43] As far as human rights violations are concerned, especially noteworthy are the Human Rights Principles and Responsibilities for Transnational Corporations, the Norms on the Responsibilities of Transnational Corporations,[44] and the Guiding Principles on Business and Human Rights, drafted in 2005 by the Special Representative of the UN Secretary-General on business and human rights and endorsed by the Human Rights Council in 2011.[45] These Principles provide a global standard for preventing and addressing the risk of adverse impacts on human rights linked to business activity.

In the specific domain of pharmaceutical business, in 2008 the UN Special Rapporteur on the right to health proposed a set of Human Rights Guidelines for Pharmaceutical Companies in relation to

[41] Stephen N. Ratner, 'Corporations and Human Rights', 111 *The Yale Law Journal* (2001) 443–545, p. 462.
[42] *See ibid.*, pp. 475–488, for an exhaustive discussion touching upon international labour law, environmental law, anti-corruption law, economic sanctions, and EU practice.
[43] UN Commission on Transnational Corporations, *Draft U.N. Code of Conduct on Transna- tional Corporations*, and OECD, *Guidelines for Multinational Enterprises*, 21 June 1976.
[44] CHR, *Human Rights Principles and Responsibilities for Transnational Corporations and Other Business Enterprises* (E/CN.4/Sub.2/2002/XX/ADD.1, E/CN.4/Sub.2/2002/WG.2/WP.1/ ADD.1), 2002; Sub-Commission, *Norms on the Responsibilities of Transnational Corpora- tions and Other Business Enterprises with Regard to Human Rights* (E/CN.4/Sub.2/2003/12/ Rev.2), 13 August 2003.
[45] HRC, Resolution 17/4, 17 July 2011; OHCHR, *Guiding Principles on Business and Human Rights. Implementing the United Nations "Protect, Respect and Remedy" Framework*, New York-Geneva, 2011; *see also* OHCHR, *The Corporate Responsibility to Respect Human Rights. An Interpretive Guide*, New York-Geneva, 2012.

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Access to Medicines.[46] Guide- lines 21–22, devoted to clinical trials, emphasise the responsibility of pharmaceutical companies to observe the internationally agreed standards:

21. A company's clinical trials should observe the highest ethical and human rights standards, including non-discrimination, equality and the requirements of informed consent. This is especially vital in those States with weak regulatory frameworks.

22. The company should conform to the Declaration of Helsinki on Ethical Principles for Medical Research Involving Human Subjects, as well as the World Health Organisation Guidelines for Good Clinical Practice.

These guidelines should be read in conjunction with Guidelines 9–14, which stress the importance of effective, transparent and accessible monitoring and accountability mechanisms. According to the Rapporteur's commentary, such mechanisms should monitor, and hold to account, pharmaceutical companies in relation to their policies and practices on clinical trials. Clearly, reference is to accountability of corporations at the domestic level and to the possibility of invoking their civil, administrative and criminal responsibility in the frame- work of national remedies.

Instead, the responsibility of corporations under international law is still *de lege ferenda*,[47] ever more so under international criminal law. In fact, although the practice following World War II has reported an increasing incidence of widespread or mass victimisation of civilians by non-state actors, especially in the domain of crimes against humanity, international criminal responsibility has been extended to non-state actors only with regard to those entities replicating the structure and organisation of a State, or exercising the same authority or control over territories and people as the one exercised by State authorities, or having the power to adopt and implement a State-like 'policy' (*e.g.* paramilitary units and bands of armed civilians). Therefore, since the international criminal responsibility of organisations and other non-state actors (legal persons, groups, corporations) is still not well-established, corporations involved in the commission of a crime against humanity normally escape accountability or punishment at the international level.[48]

[46] UNGA, *Report of the Special Rapporteur on the right of everyone to the enjoyment of the high- est attainable standard of physical and mental health* (A/63/263), 11 August 2008, Annex.

[47] HRC, *Report on the first session of the open-ended intergovernmental working group on transnational corporations and other business enterprises with respect to human rights, with the mandate of elaborating an international legally binding instrument* (A/HRC/31/50), 5 February 2016.

[48] M. Cherif Bassiouni, *Introduction to International Criminal Law: Second Revised Edition* (Martinus Nijhoff, Leiden, 2013), pp. 70–72, 132–135, 373. *See also* Nicolas Castell and Claire Derycke, 'Les entreprises', in Hervé Ascensio, Emmanuel Decaux, and Alain Pellet, *Droit international pénal* (Pedone, Paris, 2000), pp. 155–166.

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Actually, to avoid such impunity, the Rome Conference discussed the possibility to provide the ICC with jurisdiction to try not only natural persons but also legal persons, but the proposal failed to gather sufficient support.[49]

After that, a hypothetical extension of the Court's jurisdiction to include legal persons has been often debated and advocated also in recent legal literature.[50] At present, however, only individual employees, officers or directors of a corporation might be prosecuted before the ICC. Nonetheless, it was argued that Article 25(3)(A) of the Rome Statute, which provides for the criminal liability of an individual on the basis of having committed a crime 'through another person, regardless of whether that person is criminally responsible', may indirectly implicate corporations as it may provide for individual criminal responsibility for committing a crime *through* the instrumentality of a corporation.[51]

The RESPONSIBILITy of SPONSORing and HOST STATES

The involvement of States in human experimentation has progressively in- creased over time, both in terms of direct engagement in and sponsoring of medical research, and in terms of allowing foreign subjects to carry out clinical trials on their population in their territory and health facilities. Both kinds of participation in medical research raise serious concern, both for their direct involvement in ordering physicians to carry out unlawful and unethical experi- mentation, and for their failure to control and sanction such practices.[52]

States hosting research and experimentation conducted by foreign corporations, or sponsored by third States, are not totally extraneous to this activity and they bear responsibility towards all the individuals under their jurisdiction for possible breaches of their fundamental human rights. In

[49] *See* Andrew Clapham, 'The Question of Jurisdiction under International Criminal Law over Legal Persons: Lessons from the Rome Conference on an International Criminal Court', in Menno T. Kamminga and Saman Zia-Zarifi (eds.), *Liability of Multinational Cor- porations under International Law* (Brill, The Hague, 2000), pp. 139–195.

[50] Cristina Chiomenti, 'Corporations and International Criminal Court', in Olivier de Schut- ter (ed.), *Transnational Corporations and Human Rights* (Hart, Oxford-Portland, 2006), pp. 287–312; Mordechai Kremnitzer, 'A Possible Case for Imposing Criminal Liability on Corporations in International Criminal Law', in 8 *Journal of International Criminal Jus- tice* (2010) 909–918; Lynn Verrydt, 'Corporate Involvement in International Crimes: An Analysis of the Hypothetical Extension of the International Criminal Court's Mandate to Include Legal Persons', in Dominik Brodowski, Manuel Espinoza de los Monteros de la Parr, Klaus Tiedemann, and Joachim Vogel (eds.), *Regulating Corporate Criminal Liability* (Springer, Cham, 2014), pp. 281–294.

[51] Andrew Clapham, 'The Complexity of International Criminal Law: Looking Beyond In- dividual Responsibility to the Responsibility of Organizations, Corporations and States', in Ramesh Thakur and Peter Malcontent (eds.), *From Sovereign Impunity to International Accountability: The Search for Justice in a World of States* (United Nations University Press, Tokyo, 2004), pp. 233–252, p. 239.

[52] Bassiouni, *supra* note 1, pp. 402–403; M. Cherif Bassiouni, *Crimes against Humanity in International Criminal Law* (Kluwer, The Hague, 1999), p. 340.

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this perspective, the discussion on the ethics of delocalised clinical trials should also be developed against the background of human rights – human dignity and the rights to life and health, and not to be subjected to cruel or degrading treatment – in order to assess whether unethical trials are also unlawful under international human rights law.[53]

From this viewpoint, State responsibility stems directly from the provisions of human rights law and from the violation of any of the three different levels of obligations encompassed by the prevent-protect-fulfil paradigm. This approach is endorsed in foundational Principle 1 of the UN Guiding Principles on Business and Human Rights:

States must protect against human rights abuse within their territory and/or jurisdiction by third parties, including business enterprises. This requires taking appropriate steps to prevent, investigate, punish and redress such abuse through effective policies, legislation, regulations and adjudication.

Practical examples of these duties are provided in the UN Committee's General Comment No. 14 on the right to health, which explains the obligations stemming from Article 12 of the International Covenant on Economic, Social and Cultural Rights.[54]

The General Comment states that the 'obligation to respect' requires States to refrain from interfering directly or indirectly with the enjoyment of the right to health. Violations of this obligation consist in State actions, policies or laws that contravene the standards set out in Article 12 and are likely to result in bodily harm, unnecessary morbidity and preventable mortality. Examples include the failure of the State to take into account its legal obligations when entering into bilateral or multilateral agreements with other States, international organisations and other entities, such as multinational corporations. As for the 'obligation to protect', it requires States to take measures that pre- vent third parties from interfering with Article 12 guarantees. Violations of this obligation follow from the failure of a State to take all necessary measures to safeguard persons within its jurisdiction from infringements by third parties. This category includes such omissions as the failure to regulate the activities of individuals, groups or corporations so as to prevent them from violating the right to health.[55]

[53] Fidler, *supra* note 32, especially Part IV and p. 328 *et seq*.
[54] CESCR, *General Comment No. 14: The Right to the Highest Attainable Standard of Health (Art. 12)* (E/C.12/2000/4), 11 August 2000.
[55] *Ibid.*, paras. 33, 50–51.

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Another kind of responsibility incumbent on host or sponsoring States relates to their failure to prevent and repress international crimes. In this case, the responsibility stems from the violation of primary rules prohibiting certain crimes under international law and posing a positive obligation of prevention and punishment. It is a responsibility by omission, *i.e.* a responsibility which derives from the failure of the State to adopt all necessary measures, of legislative or other nature. It could be said that in the field of repression these basic obligations include the duty of the State to criminalise in domestic law the conducts prohibited under international law, the duty to adopt appropriate, effective and severe sanctions, the duty to adopt the necessary measures to establish its jurisdiction over such crimes, and, in some cases, the obligation to adopt the necessary administrative and judicial measures to ensure the presence or the detention of the accused, in order to celebrate the proceedings against them or extradite them at the request of another State.[56]

Criminologists argue that if the government fails to protect its citizens from the harm of a corporation, such behaviour should be considered a 'state-corporate crime'. Therefore, State responsibility in the domain of clinical research can also be examined in the perspective of the 'state-corporate crime' paradigm. This approach focuses on corporate crime either initiated or facilitated by the State and refers both to the collusion between State authorities and corporate business and to the failure of governmental bodies to properly regulate business and restraint deviant activities, which may depend on either their inability to protect citizens or their unwillingness to prevent and repress the harmful conduct of corporations. Unethical human experimentation can be considered a State-corporate crime in both respects, *i.e.* both when the host State is unable to protect the health and safety of the participants to the research and when it turns a blind eye to the conduct of pharmaceutical companies. Clinical trials in developing countries are considered an example of how 'the impact of the state-corporate alliance in health care has inflicted its worst damage'.[57]

Unlawful Human Experimentation in International Humanitarian Law

Given the extraordinary relevance of the Nuremberg Principles in the ethical and legal discourse on medical research, it is imperative to start the present analysis of the unlawfulness of unethical clinical trials under international criminal law referring back to the relevant

[56] *See* Linos Alexandre Sicilianos, 'La responsabilité de l'État pour absence de prévention et de répression des crimes internationaux', in *Droit international pénal*, *supra* note 48, pp. 115–128, pp. 118–121.
[57] Rawlinson and Yadavendu, *supra* note 7, pp. 10, 13. *See also* Paddy Rawlinson, 'Of Mice and Men: Violence and Human Experimentation', 2 *State Crime Journal* (2013) 72–90.

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provisions of the post-World War ii conventions on international humanitarian law. These conventions expressly criminalise biological, medical and scientific experiments and set the historical and legal reference framework for any further investigation on the qualification of unlawful human experimentation as an international crime.

This is precisely the approach adopted by M. Cherif Bassiouni in his seminal and landmark studies on this subject, which led him both to propose a definition of the international crime of 'unlawful human experimentation' regard- less of wartime[58] and to elaborate a dedicated *Draft Convention for the Prevention and Suppression of Unlawful Human Experimentation*, to be applied in all circumstances.[59]

Bassiouni's reflections on the nature of unlawful human experimentation started with the consideration that it is undoubtedly a crime in the context of war under Geneva Law, but not yet a crime under international conventional law in any other context.[60]

All four Geneva Conventions in fact criminalise torture and inhumane treat- ments 'including biological experiments' as grave breaches of the Conventions, for which States are required to provide effective penal sanctions and to bring perpetrators to court.[61] Article 12 common to the First and Second Convention strictly prohibits biological experiments, which can be subsumed under the general proscription of attempts upon the lives of the protected subjects and violence to their persons.[62] Article 13 of the Third Convention and Article 32 of the Fourth Convention prohibit

[58] M. Cherif Bassiouni, *A Draft International Criminal Code & Draft Statute for an Interna- tional Criminal Tribunal* (Martinus Nijhoff, Dordrecht, 1987), pp. 154–155 (Article IX): 'The crime of unlawful human experimentation consists of any physical and/or psychological alterations by means of either surgical operations, or injections, ingestions or inhalation of substances inflicted by or at the instigation of a public official, or for which a public official is responsible and to which the person subject to such experiment does not grant consent'.

[59] The Draft Convention was submitted to the UN Sub-Commission on the Protection of Minorities and Prevention of Discrimination by the International Association of Penal Law. Unfortunately, no action was further taken on it. In 1984 the Sub-Commission ad- opted a resolution on the *Prevention and Suppression of Unlawful Human Experimenta- tion to Promote and Protect Human Rights and Fundamental Freedoms* which appointed a special rapporteur (E/CN.4/SUB2/1984/L.21), 24 August 1984. *See* Bassiouni, *supra* note 58; M. Cherif Bassiouni, Thomas G. Baffes and John T. Evrard, 'An Appraisal of Human Experimentation in International Law and Practice: The Need for Regulation of Human Experimentation', 72 *Journal of Criminal Law & Criminology* (1981) 1597–1666. The advan- tages of a dedicated convention are thoroughly explained in Bassiouni, *supra* note 1, p. 418.

[60] M. Cherif Bassiouni, *The* Ratione Materiae *of International Criminal Law*, in M. Cher- if Bassiouni (ed.), *International Criminal Law*, Vol. I: *Sources, Subjects and Contents* (Martinus Nijhoff, Leiden, 3rd ed., 2008), pp. 129–204, p. 148; Bassiouni, *supra* note 48, p. 204.

[61] Convention (I) for the Amelioration of the Condition of the Wounded and Sick in Armed Forces in the Field, Geneva, 12 August 1949, Art. 50; Convention (II) for the Amelioration of the Condition of Wounded, Sick and Shipwrecked Members of Armed Forces at Sea, Art. 51; Convention (III) relative to the Treatment of Prisoners of War, Art. 130; Conven- tion (IV) relative to the Protection of Civilian Persons in Time of War, Art. 147.

[62] Also the rule which forbids the creation of conditions exposing the wounded, sick or ship- wrecked to contagion or infection, equally appearing in Article 12, is strictly related to this prohibition.

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scientific or medical experiments that are not justified on medical grounds and are not carried out in the interest of the affected persons.

Neither the Conventions nor their commentaries define 'biological experiment' and 'medical or scientific experiments', nor do they make any distinction between them, thus leaving space to considerable overlap between these concepts.[63] Only the recently adopted Commentary on the First Convention explains that 'in its ordinary meaning, the term "biological experiment" refers to conduct the primary purpose of which is to study the effects, at that time unknown, of a product or a situation (*e.g.* extreme cold or altitude) on the human body'.[64]

No definition of medical or scientific experiments is equally to be found in Additional Protocol I to the Geneva Conventions.[65] However, since the Protocol takes stock of the bioethical debate that was gaining momentum at the time of its drafting, it makes a distinction between 'medical procedures' and 'medical experiments'. Therefore, while Article 11(1) forbids 'any medical procedure which is not indicated by the state of health of the person concerned and which is not consistent with generally accepted medical standards', Article 11(2)(B) bans medical or scientific experiments regardless of any con- sent granted by the interested person.[66] Any wilful violation of these prohibitions or '[a]ny wilful act or omission which seriously endangers the physical or mental health or integrity of any person who is in the power of the Party other than the one on which he depends' are considered grave breaches of the Protocol under Article 11(4).[67]

The Commentary on the Protocol offers some useful guidance on the scope of the said distinction and defines a 'medical procedure' as 'any procedure which has the purpose of influencing the state of health of the person under- going it'.[68] According to the Commentary, the term 'medical

[63] The Commentary on Article 13 of Convention III and the Commentary on Article 32 of Convention IV limit themselves to stating that these experiments are 'a particularly reprehensible form of attack on the human person' and are 'certainly injurious to body or health'. *See* ICRC, *Commentary on the Third Geneva Convention*, 1960, pp. 140–141, 627; *Commentary to the Forth Geneva Convention*, 1958, p. 598.

[64] ICRC, *Commentary on the First Geneva Convention* (CUP, Cambridge, 2016), para. 1414. The three material elements which are cumulatively necessary for the grave breach of biologi- cal experiment are enlisted *ibid.*, paras. 2986–2996).

[65] Protocol Additional to the Geneva Conventions of 12 August 1949, and relating to the Pro- tection of Victims of International Armed Conflicts (Protocol I), 8 June 1977.

[66] Article 11 is the first relevant provision in international humanitarian law to mention the consent of the affected subject.

[67] On the contrary, similarly to Article 12 common to the First and Second Convention, Article 12 of Additional Protocol II STRICTLY prohibits any attempt upon the lives or physical integrity of protected persons, requiring in particular that they be not subjected to torture or to biological experiments.

[68] ICRC, Yves Sandoz, Christophe Swinarski, and Bruno Zimmermann (eds.), *Commen- tary on the Additional Protocols of 8 June 1977 to the Geneva Conventions of 12 August 1949* (Martinus Nijhoff, Geneva, 1987), p. 154, para.

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procedure' also covers any surgical operation, medication, diets or courses of treatment prescribed for medical reasons. To be authorised, a medical procedure must fulfil two cumulative conditions: its reason must be the improvement of the state of health of the person concerned or the relief of his suffering, and it must be consistent with generally accepted medical standards (*e.g.*, the universally recognised principle that medical procedures must be performed in the interest of the patient).[69] 'Medical or scientific experiments' are not separately defined but they are included among those medical procedures which 'can easily give rise to abuse and which are in principle prohibited', which is the reason why consent cannot be invoked as a defence.[70] In light of the possible exception foreseen by paragraph 1 – *i.e.* that the act is justified when it is conducive to improving the state of health of the person concerned – the Commentary clarifies that experiments carried out purely for scientific purposes are in any case categorically excluded. A marginal hypothesis in which a medical experiment might be allowed could be the case of a doctor trying out a new cure on a person who definitely could not be cured through the known methods.[71]

The 2016 Commentary on the First Convention further elaborates on the absolute nature of the prohibition on biological experiments and its scope. It stresses the irrelevance of consent, as already codified in Article 11(2) of Additional Protocol I, but also confirms that the prohibition does not prevent doc- tors in charge of wounded and sick persons from trying new therapeutic methods justified on medical grounds and dictated solely by a desire to improve a patient's condition, provided that such remedies have first been satisfactorily proved to be innocuous and that they are administered for purely therapeutic purposes. This Commentary also adds that the prohibition should not be understood as outlawing therapeutic or clinical research and that patients are entitled to freely consent to drug trials aimed at improving their health, pro- vided they are offered in the same manner and under the same conditions as to regular citizens, and that the drugs to be tested are part of a therapeutic treatment for the protected person's illness.[72] This interpretation is considered in accordance with the corresponding provisions of the three other Geneva Conventions,[73] and in particular with the above-mentioned Article 13 of Convention III and Article 32 of Convention IV, which open the door to the permissibility of scientific or medical experiments performed for therapeutic purposes.[74]

474.
[69] *Ibid.*, pp. 155–156, paras. 475–476.
[70] *Ibid.*, p. 156, para. 478.
[71] *Ibid.*, p. 157, para. 481.
[72] *Commentary on the First Geneva Convention*, *supra* note 64, paras. 1414, 2996.
[73] *See*, in the same sense, ICRC, *Commentary on the Third Geneva Convention*, 1960, Ar- ticle 130, pp. 627–628; *Commentary on the Fourth Geneva Convention*, 1958, Article 147, pp. 598–599.
[74] These exceptions to the general rule, together with the earlier commentaries on the Con- ventions, none of which

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Along the same lines as the provisions discussed so far, both the Statute of the International Criminal Tribunal for the Former Yugoslavia[75] and the Statute of the ICC[76] criminalise human experimentation as a war crime.

As far as the Rome Statute is concerned, Article 8 endorses the language of the Geneva Conventions and replicates the distinction between 'biological experiments' and 'medical or scientific experiments'.[77] Under Article 8(2)(a)(ii) biological experiments carried out on any category of protected persons during an international armed conflict constitute grave breaches of the Geneva Conventions associated with torture and inhuman treatment. The prohibition covers the use of therapeutic methods not justified on medical grounds and not carried out in the interest of the affected person. The consent of the victim is irrelevant and it is not even mentioned or alluded to anywhere. The Elements of Crime require that the experiment seriously endangered the victim's physical or mental health or integrity.[78] Under Article 8(2)(b)(x)-2 and Article 8(2)(e)(xi)-2, medical or scientific experiments carried out on one or more persons during an armed conflict amount to serious violations of the laws and customs of war applicable in international and non-international armed conflict. In this case, too, the prohibition covers experiments not justified on medical grounds and not performed for the direct benefit of the subject. The Elements of Crimes require that the experiment caused death or seriously endangered the physical or mental health or integrity and that the person was in the power of an adverse or different party to the conflict.[79] In this case, too, consent can- not be invoked as a defence.[80]

Despite the importance of these provisions, which specifically bring this odious crime under the

mentions the issue of consent, are considered in contrast to the spirit of the Nuremberg Code: *see* Aurey, *supra* note 15, p. 264.

[75] Statute of the International Criminal Tribunal for the Former Yugoslavia, adopted by Security Council resolution 827 (2003), Art. 2(b) (Grave breaches of the Geneva Conventions of 1949); Rome Statute, Art. 8 (War crimes). So far, there has been no indictment concerning this crime.

[76] Rome Statute of the International Criminal Court, 17 July 1998, entered into force on 1 July 2002.

[77] *See* William A. Schabas, *International Criminal Court: A Commentary of the Rome Statute* (OUP, Oxford, 2nd ed., 2016), pp. 246–247; *see also* Michael Cottier, William J. Fenrick, Patricia Viseur Sellers, and Andreas Zimmermann, 'Article 8: War Crimes', in Otto Triff- terer (ed.), *Commentary on the Rome Statute of the International Criminal Court: Observers' Notes Article by Article* (Nomos, Baden-Baden, 1999), pp. 173–262, p. 183; Michael Bothe, 'War Crimes', in Antonio Cassese, Paola Gaeta and John R.W.D. Jones (eds.), *The Rome Statute of the International Criminal Court: A Commentary* (OUP, Oxford, 2002), Vol. I, pp. 379–426, p. 393.

[78] Elements of Crime, Official Records of the Assembly of States Parties to the Rome Statute of the International Criminal Court, First session, New York, 3-10 September 2002, War Crimes, Article 8(2)(a)(ii)-3, War Crime of Biological Experiment, paras. 1-3.

[79] *Ibid*., Article 8(2)(b)(x)-2, War crime of medical or scientific experiments; Article 8(2)(e) (xi)-2, War crime of medical or scientific experiments, paras. 1–4. *See* Cottier et al., *supra* note 77, pp. 216–217, 283; Bothe, *ivi*, pp. 395–397, 422; Schabas, *ivi*, pp. 246–247.

[80] Elements of Crime, footnote 46.

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jurisdiction of the ICC and protect vulnerable persons from possible abuses of physicians and researchers in war time, their inherent limit is the requisite existence of an armed conflict and, as a consequence, their inapplicability in times of peace.[81] This aspect has been aptly stressed and put in relation to the principle of legality of crimes (*nullum crimen sine lege*). The consequence is that unlawful human experimentation cannot be considered an international crime in times of peace unless it amounts to other crimes, such as genocide (a condition which resembles more the pattern of Nazi experimentation than today's medical research), or crimes against humanity, including torture and inhumane acts.[82]

Unlawful Human Experimentation AS Crime agAINST Humanity

The argument that human experimentation may amount to a crime against humanity, in the form of inhumane acts or even torture, deserves in-depth consideration, especially in light of post-World War II practice, with a view to establishing whether unethical and unlawful clinical trials can nowadays trigger the jurisdiction of the ICC under Article 7 of the Rome Statute.

Article 7(2)(e) defines torture as 'the intentional infliction of severe pain or suffering, whether physical or mental, upon a person in the custody or under the control of the accused', while Article 7(1)(K) includes 'other inhumane acts of a similar character intentionally causing great suffering, or serious injury to body or to mental or physical health'. According to Bassiouni, unlawful medical experimentation in its cruellest forms clearly falls under this latter category of crime, but it may also 'cross the line of torture when no useful scientific purpose is served and the subject is transformed into a suffering victim'.[83]

Introducing Article 7, the Elements of Crime state that:

Crimes against humanity as defined in Article 7 are among the most seri- ous crimes of concern to the international community as a whole, war- rant and entail individual criminal responsibility, and require conduct which is impermissible under generally applicable international law, as recognized by the principal legal systems of the world.

'attack directed against a civilian population' has to be interpreted as a course of conduct involving the multiple commission of acts referred to in Article 7, paragraph 1, of the Statute

[81] *See also* Aurey, *supra* note 15, p. 263.
[82] M. Cherif Bassiouni, *Crimes Against Humanity: Historical Evolution and Contemporary Application* (CUP, Cambridge, 2011), pp. 419–424.
[83] Bassiouni, *supra* note 1, pp. 403, footnote 33, 411, 419.

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against any civilian population, pursuant to or in furtherance of a State or organizational policy to commit such attack. The acts need not constitute a military attack. It is understood that 'policy to commit such attack' requires that the State or organization actively promote or encourage such an attack against a civilian population.[84]

They also clarify that a State or organisational policy which targets a civilian population can be implemented either by action or, in exceptional circum- stances, by a deliberate failure to take action, which is consciously aimed at encouraging such attack.[85]

Some forms of unethical experimentation can indeed be subsumed under crimes against humanity because they meet the basic requirements and feature indicated in the Elements of Crime. The first requirement, impermissibility under general international law, is satisfied when clinical research is contrary to the principle of human dignity, non-derogable human rights and the principles enshrined in the Nuremberg Code and the DoH, which are considered already part of customary law.[86] As for the requisite nature of 'attack directed against a civilian population', this requirement is equally satisfied be- cause the offence does not ordinarily amount to a sporadic or isolated event, but is part of a wide pattern of misconduct (*e.g.*, a research protocol involving large numbers of subjects), and the victims are indeed civilians. Considering the crucial element of the systematic nature of the crime, it can be argued that human experimentation reaches the threshold of a crime against humanity when it is part of a widespread practice tolerated, acquiesced or facilitated by the government or other State authorities, as is the case with clinical research conducted on a massive scale and approved by public ethics committees and health authorities of host or sponsoring States. Massive clinical trials which are unethical and contrary to the most fundamental human rights can no doubt be considered as a widespread attack against a civilian population and the required 'policy' consists in the State encouraging and promoting such experimentation, either directly engaging in the tests, or allowing foreign subjects to carry out the research in its public health facilities, or omitting to prevent, control and regulate the action of sponsoring countries or corporations.

In such a complex scenario, all individuals involved in the performance of the unlawful

[84] Elements of Crime, Article 7, Introduction, paras. 1, 3.
[85] *Ibid*, footnote 6.
[86] *See* Bassiouni, *supra* note 1, p. 417; Jonathan Todres, 'Can Research Subjects of Clinical Tri- als in Developing Countries Sue Physician-Investigators for Human Rights Violations?', 16 *N.Y. Law School Journal of Human Rights* (2000) 737–768, pp. 750–751; Noëlle Lenoir and Bertrand Mathieu, *Les normes internationales de la bioéthique* (Presses Universitaires de France, Paris, 2004), p. 19.

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experimentation might be judged by the ICC under Article 7 of the Rome Statute, be they public officials or private individuals, since it is asserted that crimes against humanity can be also committed by civilians against civilians. In fact, according to the late Judge Antonio Cassese, the Elements of Crime generally limit the scope of crimes against humanity under customary law and also unduly restrict their notion.[87] According to him, the broadening of the scope of the customary rules on crimes against humanity now implies that these crimes may also be perpetrated by private individuals, provided they act in unison and with a common purpose and design, as if they were complying with a general state policy, in conditions where the government approves or tolerates/condones their action or where such a misbehaviour fits into a widespread practice directed against civilians of any nationality.[88] The consequences of this approach are particularly significant, since it opens the door to the possibility of invoking the international criminal responsibility of physicians and researchers who are not acting as public officials, as well as of the directors and officers of the sponsoring pharmaceutical corporations.

5. Seventy Years Later: Unethical Clinical Research and International Criminal Law

Seventy years after the adoption of the Nuremberg Code, the legacy of its principles is firmly rooted in medical ethics but the reality of human experimentation has significantly changed. Clinical research is nowadays mainly sponsored by pharmaceutical corporations and responds to their vested interests. When profit-driven experimentation is delocalised in developing countries to take advantage of lax regulation and the vulnerability of research subjects, it is imperative that all involved actors, including co-sponsoring and host States, are held accountable for human rights violations and crime. At the international level, the current legal framework applicable to private corporations is still work in progress, although there is a growing tendency to impose respect for globally accepted standards concerning business and human rights, and arguments have often been voiced for the creation of international obligations binding on them. On the contrary, governments are definitely responsible for the violation of the legal obligations stemming both from biolegal binding instruments and from international human rights law. In the perspective of international criminal law, while corporations still benefit from an account- ability gap, Article 7 of the icc Statute, interpreted in harmony with the evolving customary law on crimes against humanity, can be applied to a broad range of liable individuals involved in the performance of massive and particularly

[87] Antonio Cassese, *International Criminal Law* (OUP, Oxford, 2003), p. 93. 88
[88] *Ibid*., pp. 83, 90–91.

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serious unethical clinical trials.

International criminal law can play a prominent role in the repression of injurious medical practices disrespectful of the principles of bioethics and fundamental human rights, so as to protect both individuals and humanity as a whole from the risks associated with the criminal exploitation of advances in medical research.[89] Criminalisation of medical misconduct constituting a serious attack on the dignity, safety and physical integrity of human beings is in fact considered a crucial instrument to support compliance with ethical principles and human rights law, in accordance with the 'prescription-proscription paradigm'.[90]

Building on this assumption, international criminal law should be further developed in parallel with scientific advances and in harmony with bioethics, in order to better serve the interests of the legality and integrity of biomedical research and practice.

Nearly twenty years ago, Noëlle Lenoir questioned herself about the future of the 'international criminal law of bioethics' (*droit international pénal de la bioétique*) and the need to identify which international jurisdiction would have *ratione materiae* competence on crimes related to medical interventions contrary to the most fundamental and non-derogable principles of bioethics.[91] Given the absence of specific prohibitions, she considered the possibility of resorting to well-established international crimes foreseen in the Rome Statute (*e.g.*, prevention of birth within one group as amounting to genocide, tortures and forced pregnancies as amounting to crimes against humanity, non-consensual and unjustified medical experimentation and treatments as amounting to war crimes), but she observed that punishment of such crimes would be limited to situations of armed conflict or to systematic and wide- spread violations. To avoid the risk of 'delocalisation' of unethical practices in countries with lack of regulation and control, she advocated the drafting of dedicated conventions mirroring the consensus of the international com- munity on the need to prevent and repress transnational organised crime in ethically-sensitive fields. Such conventions, in her view, could at least enhance legislative harmonisation in the field of bioethically-related crimes, especially in three crucial domains: human cloning, organ trafficking and human experimentation.[92]

[89] *See* Aurey, *supra* note 15, p. 263.
[90] Bassiouni, *supra* note 60, p. 157: 'where human rights is the shield, ICL is the sword'.
[91] Noëlle Lenoir, 'Le droit international pénal de la bioéthique', in *Droit international pénal*, *supra* note 48, pp. 405–415, p..
[92] *Ibid.*

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While in the field of organ trafficking a remarkable achievement has been recently reached with the adoption of the Council of Europe Convention against the Trafficking in Human Organs,[93] the time seems to be ripe, given the increasing relevance that medical and pharmaceutical research has pro- gressively gained, paralleled by the emergence of new forms of human exploitation, to make Cherif Bassiouni's *Draft Convention for the Prevention and Suppression of Unlawful Human Experimentation* revive and form the object of serious and up-to-date discussion within an appropriate international forum.

Since Nuremberg, human experimentation has been the focus of the first widely-agreed principles of medical ethics ever endorsed in international law, as well as of specific prohibitions formulated in the field of humanitarian law. Nowadays, it is still the object of debate, and the cruellest and most inhumane forms of unlawful human experimentation are definitely considered *jus cogens* crimes,[94] although they are not at all comparable to the horrors of the past. Moreover, while in the Nazi experiments the elements of racial hatred and persecution were both evident,[95] modern clinical research outsourced in developing countries, albeit unethical, lacks any genocidal intent and is clearly driven by profit and exploitation. Nonetheless, under the circumstances explained above, today's massive clinical trials can amount to a crime against human- ity and trigger the jurisdiction of the ICC over public officials of host States, individual physicians and researchers acting in their private capacity, as well as officers and directors of sponsoring pharmaceutical corporations.

As is the case for human experimentation, also other unethical and unlawful medical practices performed in times of peace may be subsumed under the umbrella category of crimes against humanity, despite the absence of specific international criminal rules prohibiting them. Human experimentation is probably the field which has most contributed to 'paving the way for the biolaw path of international criminal law' and along these lines, as this Special Issue testifies, scholars are moving forward in the systematic legal construction of bioethically-sensitive international crimes.[96]

[93] Convention against Trafficking in Human Organs, CETS No. 216, Santiago de Compostela, 25 March 2015. On this topic, *see, e.g.*, Stefania Negri, 'Transplant Ethics and the Inter- national Crime of Organ Trafficking', in Anja Matwijkiw (ed.), Special Issue on Ethics & International Criminal Law, 16 *International Criminal Law Review* (2016) 287–303.
[94] Bassiouni, *supra* note 60, p. 149.
[95] Bassiouni, *supra* note 82, p. 442.
[96] *See also* Anja Matwijkiw, 'Ethics in the Making – From Controversy to Criterion for Inter- national Criminal Law', in Matwijkiw (ed.), *supra* note 93, 177–200.