Special issue

Informed consent for clinical research in the context of the Covid-19 pandemic between bioethics and biolaw: a general overview

Laura Palazzani*

ABSTRACT: The article examines the transformations of informed consent in the context of the Covid-19 pandemic, analysing the bioethical discussion and in particular the national and international documents relevant to bioethical and biolegal issues, in both institutional bodies and bioethics committees. Informed consent is analysed in the context of experimentation with treatments and vaccines, the use of biological samples and the processing of personal data.

KEYWORDS: Bioethics, biolaw, biological samples, data protection, informed consent

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1. Research in emergency and pandemic conditions: bioethical and bio-juridical aspects

The Covid-19 pandemic has given a strong impetus to clinical research, with the aim of finding a treatment, prevention or cure in the shortest possible time to safeguard public health. These are "extraordinary" circumstances, characterized by uncertainty but also by a significant amount of pressure on research; this pressure has caused a climate of confusion and stress in both research workers and participants. In this context, a bioethical discussion and a bio-juridical reflection on informed consent has arisen, with particular reference to research in pandemic emergency conditions, with regard to treatments, cures and vaccines.

Even in the context of a non-emergency situation, informed consent to participate in research is not simple. The pressure of time can make it difficult to explain essential elements in clear and

* *Full Professor of Philosophy of Law, Libera Università Maria Ss.ma Assunta (LUMSA), Roma; Vice-Chair of the Italian Committee for Bioethics; Member of the European Group on Ethics and New Technologies; Member of the UNESCO International Bioethics Committee (IBC). Mail: palazzani@lumsa.it.* *This essay is developed within the European project "Improving the guidelines for Informed Consent, including vulnerable populations, under a gender perspective" (i-CONSENT), funded by the European Union framework program H2020 (Grant Agreement n. 741856). The article was subject to a double-blind peer review process.*

understandable language. Language barriers and inadequate cultural preparation can themselves cause difficulties in communication and comprehension[1].
Starting from the aspects already present in the regulatory and bioethical context, it is crucial to highlight the emerging elements of specificity relating to informed consent with reference to the Covid-19 pandemic.

2. Regulations for experimentation in emergency conditions: the reference regulatory framework

There are already more or less binding regulatory indications and international ethics on the topic of research in emergency conditions that also constitute the reference framework for reflection on informed consent in the context of the pandemic. These are regulations that generally emphasize the possibility of doing research on human subjects, even if they are unable to give informed consent or if urgent external conditions do not make it possible to request consent.
At the international level, the *Helsinki Declaration* of the World Medical Association (2013 latest revision) accepts documented written or oral consent in emergency conditions and in the presence of witnesses, in the absence of the usual consent conditions (art.26) and "delayed/postponed" consent, upon review of an ethics committee. The document provides a framing of the problem also with reference to "unproven treatments", in the absence of effective treatments, allowing participation with information on the possibility of it offering the hope of saving life, re-establishing health or alleviating suffering, with the "commitment of the researcher to give any information which may prove to be important during the research to the subject" (art.37).
Another source is the Council for International Organizations of Medical Sciences (CIOMS), *International Ethical Guidelines for Health-related Research Involving Humans*, Guidelines 20 (2016), which explicitly refers to the pandemic[2], stressing the need, in such emergency conditions, to change standard procedures, while observing ethical principles. The document identifies a path, which may prove necessary, to accelerate the ethical review of research to facilitate relevant studies that can begin as soon as possible without compromising ethical requirements.
Even the *Universal Declaration of Bioethics and Human Rights* of UNESCO (2005), although it does not explicitly address the problem, indicates in art.8 - dedicated to respect for human vulnerability and personal integrity that in the application and advancement of scientific knowledge, medical practice and associated technologies, the vulnerability of the human person must be taken into account and provide for specific protection for individuals and groups in situations of particular difficulty, as well as respect for their personal integrity.

[1] As highlighted in L. PALAZZANI (edited by), *Special Issue on iConsent - Improving the Guidelines for Informed Consent, Including Vulnerable Populations, Under a Gender Perspective*, in *BioLaw Journal-Rivista di BioDiritto*, Special Issue 1/2019, pp. 154.
[2] CIOMS*, International Ethical Guidelines for Health-related Research Involving Humans* (2016), Guideline 20: "Research in disasters and disease outbreaks. In fact, an acute disaster situation can require modifying standard procedures so that ethical principles can be upheld in the most expedient way possible. For example, while ethical oversight is essential in all research, accelerated ethical review during disasters may be necessary to ensure that valuable studies can begin as soon as possible without compromising ethical requirements".

At the European level, it should be remembered that the *Additional Protocol Concerning Biomedical Research* (2005) at the Convention on Human Rights and Bioethics of the Bioethics Steering Committee of the Council of Europe justifies research in emergency conditions on humans if there is no alternative treatment of comparable effectiveness (art.5) and permits participation in research to the patient in emergency situations and not in a state to give their consent or who are able to consent when owing to the urgency there is no time to request informed consent or to obtain the authorisation of the legal representative. In such circumstances the following requirements are indispensable: the research cannot be carried out on persons in non-emergency conditions; there are no previously expressed objections; the research must be approved by an ethics committee; even when the research will not produce direct benefits, it could potentially contribute to the improvement of understanding capable of conferring benefit to the person concerned or to other persons who belong to the same category or those afflicted by the same disease or condition, entailing minimal risk and discomfort. Consent or authorization for continued participation shall be requested as soon as "reasonably possible".
Along the same lines are, the Integrated addendum to ICH E6 (R1), *Guideline for Good Clinical Practice,* (2016) and the World Health Organization, *Operational Guidelines for Ethics Committees that Review Biomedical Research* (Geneva, 2000).
Regulation 536/2014 of the European Parliament and the Council on Clinical Trials on Medicinal Products for Human Use, and Repealing Directive 2001/20 / EC (2014), dedicates art. 35 to "Clinical Trials in Emergency Situations" and establishes the ethical conditions for research as: the presence of scientific grounds consistent with the potential given by participation in relation to a direct relevant benefit in terms of the improvement of health and well-being or in reducing suffering; absence of previously expressed objections to participation; the minimisation of risk and discomfort, compared to standard care and treatment[3]. However, consent must be given as soon as possible, i.e. when the subject regains the ability to provide it. It can be expressed in unwritten form with an impartial witness and the research approval of an ethics committee.

3. Diversification of informed consent in research during the pandemic

3.1. Informed consent and experimentation in the context of the pandemic

The World Medical Association points out that research is an "ethical imperative" when public health[4] is at stake: but research must always respect scientific standards of quality and validity. The danger, in

[3] "Scientific grounds to expect that participation of the subject in the clinical trial will have the potential to produce a direct clinically relevant benefit for the subject resulting in a measurable health-related improvement alleviating the suffering and/or improving the health of the subject, or in the diagnosis of its condition"; "the investigator certifies that he or she is not aware of any objections to participate in the clinical trial previously expressed by the subject"; " the clinical trial poses a minimal risk to, and imposes a minimal burden on, the subject in comparison with the standard treatment of the subject's condition".
[4] WHO, *Ethical Standards for Research during Public Health Emergencies: Distilling Existing Guidance to Support COVID-19,* 2020, https://apps.who.int/iris/handle/10665/331507 (last accessed on June 1st, 2021); WHO, *Guidance for Managing Ethical Issues in Infectious Disease Outbreaks*, 2016, https://apps.who.int/iris/handle/10665/250580 (last accessed on June 1st, 2021); Nuffield Council on Bioethics, *Research in Global Health*

times of pandemics, could be the efforts to push towards an acceleration of research, with the temptation to skip some of the "ordinary" phases of the trial process in the context of the "extraordinary" situation created by the pandemic[5]. The Covid-19 emergency has urged all researchers to start studies and trials[6], but it is important to monitor their quality so that the rights of research participants are protected, including the right to have adequate information and to have the opportunity to express free and informed consent.

Information to research participants must be clear from the moment of *recruitment*, explaining the criteria for inclusion and exclusion, with the balancing of the risks and benefits of participation or non-participation in the research, in the awareness that at times it may be or seem riskier not to participate than to participate, in the context of the pandemic where there are no validated therapies. Recruitment must protect the most vulnerable but not exclude them, because exclusion can however deprive them of new opportunities for treatment: the so-called particularly vulnerable categories, pregnant or breastfeeding women, children, people with disabilities, immigrants, should not be excluded a priori for "protective" purposes, without a reasonable scientific and ethical justification. Recruitment also includes "frontline workers" (physicians and nurses) who personally expose themselves to risks to help patients, not only in the area of treatment and care, but also in the context of research: the principle of solidarity can justify this priority, however, adequate information regarding the risks, and an equitable distribution between risks and benefits among the research participants must always be ensured, in order to avoid forms of conscious or unconscious exploitation. Participants should be treated with respect and selected in such a way that minimizes risks, maximizing the social value of the research.

Respect for *autonomy in participation* must always be central, ensuring the freedom and voluntariness in the participant's decision and avoiding their feeling pressured to take part or even feeling guilty for not participating towards others and society in general. The context of the pandemic risks spreading the idea that every attempt must always be made, no matter what, however, we cannot expose people to unnecessary risks, with the sole aim of acquiring new knowledge. Some groups are particularly susceptible to these dynamics: for example, in China, the first large block of patients will be the military. Even in Western contexts, the military are vulnerable due to the possible reduction of autonomy owing to obligations towards those in a superior hierarchical position. Exposing participants to unnecessary risks is ethically unacceptable. Participation in research in the absence of alternatives makes the choice a particularly delicate one; it is imperative to avoid misunderstandings with the participant about the role of research, which means, clarifying the experimental nature and uncertainty of the research and proposing possible alternative paths, without resorting to forms of "experimental persistence". In the context of a severe and even fatal pandemic infection, many people may be willing to take a high risk or use unproven agents in a clinical trial or outside the framework of

Emergencies: Ethical Issues, 2020, https://www.nuffieldbioethics.org/publications/research-in-global-health-emergencies (last accessed on June 1st, 2021).

[5] In this perspective, administrative processes for reviewing research protocols must be accelerated and simplified if these protocols are related to the treatment, prevention or diagnosis of infections caused by SARS-CoV-2.

[6] CIOMS, *International Ethical Guidelines for Health-related Research Involving Humans*, Guidelines 1: Without scientific validity, the research lacks social value and must not be conducted (see Guideline 1 – Scientific and Social value and respect for rights).

a clinical trial. It is essential that researchers realistically balance potential benefits and risks and communicate them in a clear and transparent manner to potential participants. If participation in the study, in pandemic times, increases the risks for participants, this should be carefully taken into consideration, remembering that safety is a priority. The justification for *compassionate studies* must always provide an opening to the possible benefits for the patient: a study that has as its objective only the indirect benefits for society is to be considered unethical. It is also important to discourage patients from participating in studies outside clinical settings: on-line experimentation or self-experimentation involves dangers in the absence of medical supervision and monitoring.

Even if research is carried out under difficult and emergency conditions, informed consent must still be collected to the extent possible in order to ensure that those who decide to participate in the research have actually understood and evaluated the risks and benefits and are able to make a conscious and informed decision. *Informed consent remains a fundamental requirement***;** the understanding of the risks and benefits by the participant must be ascertained, avoiding, in the context of the pandemic, the perception of risks being reduced in the face of expectations that are not always reasonable[7]. Oral or photographed/video recorded consent in the presence of witnesses (selected according to impartial criteria justified by the investigator) is also acceptable; digital technologies for informed consent must be implemented (avoiding paper and improving and speeding up information for patients). When it is not possible to obtain informed consent in the usual way, due to movement restrictions or isolation of patients, alternative procedures should be considered, but as soon as the situation permits, informed consent must still be obtained. Researchers must consider the particular condition of vulnerability in the context of the pandemic, the pressure of time of the research may not coincide with the time for maturing consent: despite the external pressure, the uncertainties of the participant's decision must be respected, considering that fear, discomfort, stress can compromise the understanding of the information and the decision to participate itself. In the event of changes to protocols, which are frequent due to the evolution of the pandemic, consent must, to the extent possible, be requested again with the appropriate changes.

The World Health Organization in the document *Ethical Standards for Research during Public Health Emergencies: Distilling Existing Guidance to Support COVID-19*[8] emphasizes that informed consent, as a fundamental requirement of research even in pandemic emergency conditions, also requires an increase in responsibility on the part of researchers and ethics committees in ensuring that research activities do not proceed without a reasonable scientific basis aimed at safety and efficacy, and that risks are minimized "to the extent possible" ("to the extent reasonably possible"). An emphasized element is the *problematicity in confusing the dual role of physician and researcher***:** it is desirable for the researcher and the treating physician not to be the same person, since this dual role could exert an indirect pressure to participate on the patient, who, may fear that non-participation could lead to a loss or at least a reduction in care and attention. Furthermore, researchers and sponsors should

[7] COUNCIL OF EUROPE, COMMITTEE ON BIOETHICS (DH-BIO), *Statement on Human Rights Considerations Relevant to the COVID-19 Pandemic*, 14 April 2020, https://rm.coe.int/inf-2020-2-statement-covid19-e/16809e2785 (last accessed on May 31st, 2021).

[8] COUNCIL OF EUROPE, COMMITTEE ON BIOETHICS (DH-BIO), *Statement on Human Rights Considerations Relevant to the COVID-19 Pandemic*, cit.

ensure that individuals participating in the research can access the *possible benefits resulting from their participation*. If research results are proven safe and effective, such results should be made available to participants as soon as possible, including when possible access to drugs or interventions not yet registered, and nevertheless making, every effort to provide equitable access to the benefits of the research conducted under emergency conditions. These elements should also be included in the informed consent.

The European Medicines Agency (EMA) has also expressed its stand on the subject, together with Heads of Medicines Agencies (HMA) in the document *Guidance on the Management of Clinical Trials During the Covid-19 Pandemic* (28 April 2020) in which it is emphasized that *the sponsors* should be aware of the pressure on doctors to carefully evaluate the relevance and appropriateness of enrollment in clinical trials and that patients should be informed *of alternatives to written informed consent* (e.g. oral consent, in the presence of a witness, deferred consent, renewal of consent or reconfirmation for changes to the protocol by telephone or e-mail, to avoid participants being exposed to unnecessary risks). The informed consent obtained through these methods must be reconfirmed, through standard procedures, as soon as possible and the reasons for the impossibility of obtaining customary informed consent from the patient must be appropriately motivated and recorded by the researcher.

The European Commission has issued specific guidelines *Guidance on the Management of Clinical Trials during the COVID-19 (Coronavirus) pandemic* (2020) aimed at ensuring the conducting of *clinical trials* during the Covid-19 epidemic, given the numerous difficulties, including the restriction on visits to healthcare facilities, the scarce availability of resources all concentrated in dealing with the emergency, the need for isolation and quarantine for some participants in the studies[9]. On informed consent, it reiterates that the opportunity to obtain consent from subjects must always be given priority over other solutions, even in cases of subjects who are in isolation, for which cameras or photographs of the documentation can be used taken through the transparent isolation barriers. In the case of temporary consent in verbal form, the presence of an impartial witness is required to certify that the consent has been given and signed and dated on the informed consent document. It is up to the investigator to certify the method of selection of the impartial witness[10].

The Bioethics Committee of the Council of Europe (DH-BIO) in the document *Statement in the Context of the COVID19 Crisis* (2020) underlines how the case of "compulsory isolation" for a seriously infectious disease, such as a pandemic, falls within the exceptions to informed consent for public health protection reasons. This exception is provided for in art. 8 of the *Convention on Human Rights and Bioethics* (1997) which concerns emergency situations, which include the pandemic. The document states that in these conditions, when the appropriate consent cannot be obtained, any medical intervention that proves to be of direct benefit to the individual is possible. As part of the research, DH-BIO reiterates the requirement of respect for human rights reflected in the Oviedo

[9] European Medicines Agency (EMA), *Guidance on the Management of Clinical Trials During the COVID-19 (Coronavirus) Pandemic*, available https://ec.europa.eu/health/sites/default/files/files/eudralex/vol-10/guidanceclinicaltrials_covid19_en.pdf (last accessed on May 31st, 2021).

[10] In Italy, the Italian Medicines Agency (AIFA) has explained these guidelines on informed consent in the Communication of 12 March 2020, updated on 7 April 2020.

Convention, which does not provide for exceptions in art.16 and 17 to the protection provided for research participants (permitting as the only conditions, when there is no comparable alternative in terms of effectiveness to research on human beings, the non-disproportion of the risks compared to the potential benefits, in addition to the approval of the ethics committee). The Committee of the Council of Europe underlines how the Additional Protocol on biomedical research usefully completes the Convention in art.19 in the context of the conditions for research in emergency conditions. If the person is not in a state to give consent due to a lack of awareness and/or the urgency of the situation, consent can be given by the legal representative, with the approval of the committee and verification of the absence of explicit objection by the subject.

In the *Position of the European Network of Research Ethics Committees (EUREC) on the Responsibility of Research Ethics Committees During the COVID-19 Pandemic* (2020)[11] it is emphasized that informed consent must remain compliant with European and national regulations. It recognizes that national regulations may differ in Europe. The proposed simplification of consents in the context of the pandemic should be taken into consideration by the European ethics committees, as part of the primary objective of protecting the dignity, rights and safety of participants, patients and healthy volunteers, in the context of medical studies. The document stresses that "the pressure exerted on medical research must not lead to the research or experimentation of drugs on humans without compliance with the ethical standards applicable to medical research".

In the context of *vaccine research*, some specific aspects emerge, with regard to experimentation. The World Medical Association in the document *Key Criteria for the Ethical Acceptability of COVID-19 Human Challenge Studies* (2020) returns to the topic (after the document *Human Challenge Trials for Vaccine Development: Regulatory Considerations*, 2016) addressing the specific issue of vaccine testing through studies with intentional controlled infection of healthy volunteers, with a dose high enough to cause disease and thereby stimulate the immune system, but not so high as to cause disease in a severe form. These are studies that could be justified in principle given the urgency of research on vaccines, the need to accelerate research due to the speed of the spread of the virus, and its global expansion. There is a broad bioethical discussion on the issue with particular reference to the proportionality or disproportionality in balancing benefits and risks. The potential benefits of this research are: the possibility of speeding up research times; the reduction in the number of volunteers compared to the usual clinical trials that involve tens of thousands of participants, compared to numbers always lower than one hundred for *Human Challenge Trials*; the increase in information obtainable in less time; cost reduction. But certainly the risks are high since there is no cure and no proof of efficacy of the treatments available, therefore even with the risk of death for participants. The basic principle of clinical ethics should be remembered which allows experimentation on condition that there is a minimizing of the risks for subjects and maximizing of the benefits: by their nature, the *Human Challenges Trials* would seem to contradict this fundamental precept. The World Medical Association underlines certain ethical requirements, while opening to this possibility albeit in a limited way under certain conditions, including also informed consent, which must be particularly rigorous

[11] *Position of the European Network of Research Ethics Committees (EUREC) on the Responsibility of Research Ethics Committees During the COVID-19 Pandemic*, 2020, http://www.eurecnet.org/documents/EUREC_Positionpaper_March_2021.pdf (last accessed on May 31st, 2021).

due to the potentially high risk and uncertainty, the complexity of the information that must be properly understood. Consent must be reviewed during the study when new relevant risk data are available after the study has begun. The selection of participants at the time of enrollment must include full understanding of the potential risks and voluntariness: in this sense, those who come from difficult social backgrounds must be excluded precisely because of the risk of an inadequate understanding and the possibility of their exploitation for scientific advantage. The document insists on the need for scientific justification for the research, which must be able to produce relevant results for public health and which cannot be obtained in another less risky manner, on the importance of a preliminary systematic risk assessment (quantification of risks, comparison with other studies, clarification strategies to minimize risks) and on the relevance of transparent public involvement of research participants, the guarantee of long-term monitoring, the international coordination of research, the ethical review of experts. In addition, it also insists on comprehension tests, which make it possible to verify the acquisition of full awareness regarding the choice. The ethical reservations about these studies concern, in the light of the bioethical principle of the primacy of human dignity over the interest of science (shared by international bioethics and bio-law), the acceptability of the sacrifice involved in the exposure to risks for the community by subordinating personal good to public good, the duty of the researcher to intervene on subjects only in a proportionate way as well as the problematic nature of reimbursements or even compensation that call into question the bioethical principle of free participation and the prohibition of the sale or purchase of the body (exposing poor people to disproportionate risks purely for economic objectives).

3.2. Consent to the use of biological samples

In the context of the pandemic, specific issues arise in relation to informed consent for biological samples.

It should be specified to the subject whether the samples, taken using different methods, *are for diagnostic purposes only or also for research purposes.* The possibility of tests for the diagnosis of the presence or absence of the infection is an opportunity for individuals and for the community, but it must not hide research paths. The purposes of the test must be clarified in the consent, specifying whether it is an epidemiological study, a health surveillance on specific populations for public health purposes, a screening test, a diagnostic test and/or biobanking. The possibility of biobanking must be made explicit in the consent, with clarifications - as for any research - on the time and purpose of the research, on the possible destruction or preservation of the samples for future use, making it clear that it is directly or indirectly related to Covid-19 research. The storage location of the biobank and any transfer abroad of the biological material should also be specified, including specification of adequate privacy guarantees[12]. What is collected, where it is collected, how it is collected, for what purposes, and for how long must be made clear. It should also be specified whether the samples will be pseudo-anonymized (in accordance with current legislation) and in the case of interruption of the research (by

[12] ISTITUTO SUPERIORE DI SANITÀ, ISS COVID-19, *Translational Research Working Group 2020, Recommendations for collection, transport and storage of COVID-19 biological samples*. Version of April 15, 2020., pp. 19, https://www.iss.it/documents/20126/0/Rapporto+ISS+COVID-19+n.+13+campioni+EN.pdf/19533b9b-a811-ce0e-a631-e64b040bca77?t=1589362071454 (last accessed on June 1st, 2021).

the researcher or the participant) whether these will be destroyed or anonymized. Researchers should make information public as soon as it becomes available. It should be specified whether genetic analyzes will be carried out as well as any possible strategies in the event of "unexpected results", i.e. results not expected but of clinical relevance for prevention, diagnosis or treatments.

A specific question emerges in relation to *mandatory or voluntary testing*: mandatoriness can be diversified to *varying degrees and forms*; voluntariness can indicate *different situations* (e.g. it is one thing if the test is proposed by the health facility to its employees, and another thing if it is requested by the person concerned for his/her own purposes). It must be specified in the consent if the request for the test comes from the interested party or if it comes from institutions for health surveillance and/or public health purposes. It is necessary to ensure the availability of material - i.e. serological test kits and swab reagents - for tests required for public health purposes (such as those carried out on healthcare professionals) and for urgent clinical purposes.

The Word Health Organization in the document *Ethical Standards for Research During Public Health Emergencies: Distilling Existing Guidance to Support COVID-19* stresses that researchers should inform potential participants about the circumstances in which biological samples may be shared. In the context of the pandemic the sharing of biological samples becomes a possibility which participants and stakeholders must be informed of. To the extent that samples have the potential to generate responses that are useful to public health, there is an ethical obligation to share the information. Given the urgency of the research, consent can be broad and dynamic, open to future research uses of the samples. The sharing of biological samples can/should be a viable option[13] alongside the option of biological sample control (restricted consent). Sharing takes on a humanitarian and supportive value for the future of research, in helping to reduce the suffering of present and future patients. It is the responsibility of the researcher and the ethics committee to verify that the consents are understandable and avoid the risks of harm and exploitation of those who already suffer disadvantages and hardships. The ethical conditions for sharing samples must be equitable and responsible: equitable, means allowing equal access to benefits; responsible, means ensuring that sharing is effective and safe. In this sense, public information on the importance of research on biological samples would be desirable. In the event of a denial, the samples must be anonymized and destroyed once the purpose for which they were collected in the emergency has been finalized. Similarly, samples must be anonymized in the event of the patient's death, in the absence of his/her explicit consent to Covid-19 biobanking.

At the European level as at the national level, there is no regulation specifically dedicated to research biobanking, but research on biological samples is regulated in a contextual manner to the regulation on data processing for scientific purposes[14].

[13] COMITÉ DE BIOÉTICA DE ESPANA*, Informe sobre los requisitos ético-legales en la investigatcion con datos de salud y muestras biologicas en el marco de la pandemia de Covid-19*, April 2020, http://assets.comitedebioetica.es/files/documentacion/Informe%20CBE%20investigacion%20COVID-19.pdf (last accessed on June 1st, 2021).

[14] To represent the ethical-regulatory set-up of informed consent to research biobanking, also using the tool of analogy, both legislative acts with binding legal value (European Regulation, Directive; Legislative Decree, Provision, Authorization, etc.) and documents (Recommendation, Convention, Declaration, etc.) are proposed in order to direct, recommending good practices but these are not binding.

The Convention on Human Rights and Bioethics (Oviedo 1997) of the Council of Europe explicitly states: "when a part of the human body is removed in the event of an intervention, it cannot be preserved and used for purposes other than those for which it was collected and in accordance with appropriate information and consent procedures". The *Recommendation 2006/4* of the Council of Europe, replaced and updated, by the *Recommendation 2016/6 on Research on Biological Materials of Human Origin* specifies the defense of physical integrity and privacy; the right of every individual to accept or refuse to contribute to research; transparency of governance; the minimization of the physical risk of the withdrawal and risk to private life (for the individual and the family) and the proportion with respect to the benefits obtainable from the research (risks per group of individuals); the refusal to give consent or the withdrawal of consent to collection and use for research must not lead to any discrimination (in particular in the context of the right to treatment); the gratuity of the donation; the anonymization and use of identifiable samples must be justified in the research and evaluated by an ethics committee; the spread of research knowledge; the traceability of biological materials. The recommendation states that biological materials can be removed from the body of a deceased person to be kept for future research only with the consent or authorization required by law, preceded by adequate information, including on the right to refuse. Additionally, biological materials should not be removed to be stored for future research if the deceased person is known to have objected to their post-mortem preservation.

In the context of the Italian regulation on post-mortem research biobanking, reference can be made to Law 10 February 2020, n. 10 *Rules on the disposition of one's body and post-mortem tissues for study, training and scientific research purposes*. The modalities and requirements of consent to the post-mortem donation of one's own body and parts of the body (biological samples) are established by article 3: the declaration of consent must be drawn up, in analogy with the Law 219/2017 on informed consent and on advance treatment directives, in the forms provided for by the directives for advance treatment, that is to say by public act, by authenticated private act, or by private act delivered personally by the subscriber to the civil status office of the municipality of residence. Furthermore, the declaration of consent must be delivered to the Local Health Authority to which he/she belongs, which is responsible for keeping it and electronically transmitting it to the Advance Treatment Directive Database. Withdrawal of consent can be done at any time in the same way. Unlike Law 219/2017, the declaration of consent for post-mortem donation requires a trustee to be appointed who is responsible for communicating the existence of the consent to the doctor ascertaining the death.

3.3. The right to privacy and protection of personal data and informed consent

The collection of data as part of participation in research in the context of the pandemic must be fast and accurate, according to the criteria of *quality, accessibility, transparency, standardization, interoperability. Data protection* must be guaranteed, but it must not prevent measures against the pandemic, since the fight against the pandemic is a value shared by all nations, in the interest of all humanity.

The (EU) Regulation 2016/679 of the European Parliament and of the Council of 27 April 2016, *General Data Protection Regulation*, allows, in exceptional circumstances such as an epidemic and for reasons of public interest, temporarily to process data having the public interest as a legitimate legal basis of

the processing, even in the absence of consent. This does not relieve the data controllers and processors from protection of the personal data of the persons involved, but the emergency is recognized as a "legal condition that can legitimize restrictions on freedoms by providing for proportionate and limited restrictions in time" and even exemptions to privacy. The necessity, proportionality, appropriateness of such exceptions, in the context of a democratic society, must comply with the Charter of Fundamental Rights of the European Union (2000) and the *European Convention for the Protection of Human Rights and Fundamental Freedoms* (1958) subject to the control of European Court of Justice and the European Court of Human Rights. Each measure must be properly documented.

The European Data Protection Board (EDPB) in the document Statement by the EDPB Chair on the Processing of Personal Data in the Context of the Covid-19 Outbreak, adopted on March 16, 2020, clarifies that these restrictions must be proportionate and confined to the period of emergency, and that in any case, the data controllers and processors must ensure the protection of the personal data of the data subjects. In particular, the Committee affirms that the personal data necessary to achieve the objectives pursued should be processed *for specific and explicit purposes,* the data subjects should receive *transparent information* on the processing activities carried out and their main characteristics, including the retention period of the collected data, the information should be easily accessible and formulated in simple and clear language, the measures put in place to manage the current emergency and the related decision-making process must be adequate and documented.

The Joint Statement on the Right to Data Protection in the Context of the COVID-19 Pandemic (by Alessandra Pierucci, Chair of the Committee of Convention 108 and Jean-Philippe Walter, Data Protection Commissioner of the Council of Europe Strasbourg, 30 March 2020), underlines that the guiding ethical principle must remain the primacy of the human being and the adoption of professional standards in the use of health data in the guarantee of fundamental rights and freedoms, with particular reference to the right to privacy. The sharing of data in the context of health professionals must be allowed; in the context of public communication by the authorities, data on the health of specific individuals should be avoided[15].

The DH-BIO Bioethics Committee at the Council of Europe in the *Statement in the Context of the COVID19 Crisis* (2020) recalls art. 10 of the *Oviedo Convention* concerning the right to privacy of information in the field of health, reaffirming the principle introduced in art. 8 of the *European Convention for the Protection of Human Rights and Fundamental Freedoms.* The possibility of this restriction on the exercise of rights including the right to privacy is explicit in art. 26. These exceptions are aimed at collective protection and safeguarding public health. But such restrictions must be

[15] *Joint Statement on the right to data protection in the context of the COVID-19 pandemic by Alessandra Pierucci, Chair of the Committee of Convention 108 and Jean-Philippe Walter, Data Protection Commissioner of the Council of Europe*, 30 March 2020, https://www.coe.int/en/web/data-protection/statement-by-alessandra-pierucci-and-jean-philippe-walter (last accessed on June 1st, 2021); EUROPEAN DATA PROTECTION BOARD, *Statement on the Processing of Personal Data in the Context of the COVID-19 Outbreak*, 19 March 2020, https://edpb.europa.eu/news/news/2020/statement-processing-personal-data-context-covid-19-outbreak_en (last accessed on June 1st, 2021). See also RESEARCH DATA ALLIANCE (RDA), *COVID-19 Working Group, Recommendations and Guidelines*, 15 May 2020, https://www.rd-alliance.org/15-may-2020-fourth-release-rda-covid-19-guidelines-and-recommendations (last accessed on May 31st, 2021).

prescribed by law in democratic societies and must be interpreted within the framework of the criteria defined by the European Court of Human Rights, in particular necessity and proportionality.

In Italy the Law Decree n. 14 of 9 March 2020, *Provisions for the strengthening of the National Health Service in relation to the COVID-19* emergency clarifies how the processing of data collected during the emergency period must take place in compliance with the principles set out in art.5 of the European Regulation 679/2016 adopting proportional measures with regard to necessity. Art. 14 of the decree law provides, until the end of the state of emergency, the possibility of simplifying some aspects of the processing of personal data for reasons of public interest in the public health sector, mentioning the diagnosis and health care of those infected, but it could also be extended to research. Paragraph 5 of the same article introduces the possibility of omitting the information or providing simplified information, after verbal communication of the limitation. Paragraph 4 allows the data controller or data processor to assign, under their own responsibility, specific tasks and functions related to the processing of personal data to individuals, expressly designated, who operate under their authority, in a simplified manner, including verbally. A report on the *Protection of personal data in the COVID-19 emergency* was prepared on the subject by the Covid-19 Bioethics Working Group no. 42 2020 (May 28, 2020).

As part of the "exemptions to consent" in a FAQ (Frequently Asked Question) published on the website of the Guarantor for the Protection of Personal Data relating to the *Processing of data in the context of clinical trials and medical research in the context of the COVID-19 health emergency*, it is indicated that, if for specific and proven reasons (e.g., impossibility of communication of information; disproportionate effort required by the procedure with the risk of making it impossible or prejudice the outcome of the research), it is not possible to acquire the informed consent of the interested party even from third parties – as in the case of treatment of data referring to deceased or hospitalized patients in intensive care units – the owners who intend to carry out data treatments concerning experimental studies and compassionate uses of medicines for human use, for the treatment and prevention of the virus, in the emergency phase they are not obliged to submit the research project prior to evaluation of impact and prior consultation of the Data Protection Authority referred to in art. 110 of the Code regarding the protection of personal data.

In compliance with the regulation on privacy (through pseudo-anonymization), in pandemic times consideration must be given to the importance of *sharing data* in the scientific community for an efficient impact of results, considering also the risks and potential damage of not sharing data: data are a precious asset and an individual contribution to the advancement of knowledge with also a potential direct benefit, in addition to the indirect benefit for society. It is essential to monitor the correct storage of data in reliable and certified public deposits, with the guarantees of compliance with regulations and ethical requirements, preventing abuses[16]. According to the World Health

[16] UNESCO International Bioethics Committee (IBC), World Commission on the Ethics of Scientific Knowledge and Technology (COMEST), *Statement on Covid-19: Ethical Considerations from a Global Perspective* (April 2020): "there is a need for coordination of international efforts and the formulation of a common understanding of ethical review processes; An oversight committee for responsible research during this pandemic on a global level needs to be urgently created". The Statement is https://en.unesco.org/themes/ethics-science-and-technology/comest (last accessed on May 31st, 2021).

Organization, the culture of sharing data and results should be the norm in health emergencies, and the decision not to share data and results should be justified by researchers and administrators at local, national and international levels.

4. The "lessons learned" on informed consent in the context of the Covid-19 pandemic

Informed consent plays an increasingly important role in allowing the patient to make an *autonomous choice,* based on full awareness and responsibility in the context of the Covid-19 pandemic. The patient must also be aware of the particular conditions of vulnerability, with an equitable and proportionate distribution of risks and benefits in order to minimize the risks, maximizing the social value of the research. The researcher's understanding of the risks must be ascertained (possibly not coinciding with that of the treating physician), avoiding, in the context of the pandemic, the perception of risks being decreased in the face of expectations that are not always reasonable and realistic. Despite external pressure, the importance of respecting the uncertainties of the participant's decision and the decision-making process emerges, considering that fear and discomfort can compromise serene patient participation. The pandemic has also prompted the spread of alternative methods to written consent (oral or photographed/video recorded consent in the presence of witnesses) as well as the implementation of the use of digital technologies speed up and improve information for patients.
In the field of biological samples, the importance of the specification of the purpose of the research is becoming increasingly evident, and the strong driving force of solidarity in the sharing of biological samples as a possible option, as opposed to the trend towards individualism. Sharing takes on a humanitarian and supportive value, as part of so-called participatory development, in the context of biomedical research given the urgency of responses for the community. Data collection in the context of participation in pandemic research must be fast and accurate, according to the criteria of quality, accessibility, transparency, standardization, interoperability. Data protection must be guaranteed, but it must not hinder measures against the pandemic, since the fight against the pandemic is a value shared by all nations, as a global interest of all humanity. There are many documents that allow "exceptions" to consent: what emerges is the importance of sharing data in the scientific community in order to achieve an efficient impact of the results for the "global common good".