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## Informed Consent. The Current Standing

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# INFORMED CONSENT. THE CURRENT STANDING

Miroslav Radenković<sup>1</sup>

## GENERAL REMARKS

Controlled research clinical trials on human subjects are aimed to test new drugs, involving individual patient recruitment, randomization, and follow-up; they also need to be supported by suitable ethical principles and regulatory background.<sup>2</sup> That way, it is well-accepted that fundamental prerequisites for any ethically grounded research should address the following points<sup>3</sup>:

1. Scientific validity
2. Social value
3. Minimum human risk
4. Benefits should outweigh risks
5. Informed consent
6. Protection of confidentiality and privacy
7. Equitable subject selection with scientific or moral justification for including or excluding subjects from research
8. Protection from harm or exploitation of vulnerable subjects, including children, prisoners, and mentally disabled subjects.

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<sup>2</sup> Cory E. Goldstein et al., “Ethical Issues in Pragmatic Randomized Controlled Trials: a Review of the Recent Literature Identifies Gaps in Ethical Argumentation,” *BMC Medical Ethics* 19(1) (2018), <https://doi.org/10.1186/s12910-018-0253-x>.

<sup>3</sup> David B. Resnik, “Environmental Health Research Involving Human Subjects: Ethical Issues,” *Environmental Health Insights* 2 (2008), <https://doi.org/10.4137/ehi.s892>.

9. Data integrity and safety monitoring

10. Independent review (Institutional Review Board oversight)

If we are talking about consent in general, it should be applicable to different purposes. That way, consent may be commonly labelled as implied consent, written consent, expressed consent, informed consent, proxy consent, blanket consent, or oral consent.<sup>4</sup> In particular, in research ethics, informed consent represents a course of action of acquiring the consent from the human subject to participate in clinical research after being fully informed of the research aims, study protocol, as well as predictable benefits and potential harms.<sup>5</sup> Throughout this process, a relevant ethics committee is responsible for assuring that the research itself will be conducted in complete accordance with the study plan, adopted methodology, and the highest ethical standards.<sup>6</sup>

Obtaining informed consent from participants in clinical research is essential because it promotes their welfare and ensures their rights.<sup>7</sup> That way, essential ethical principles underlying research on human subjects, specifically autonomy, beneficence, nonmaleficence, and justice, need to be followed.<sup>8</sup> Consequently, we should always be reminded that three essential standards for clinical informed consent must be appreciated: the patient must be competent, adequately informed, and not coerced.<sup>9</sup>

It is therefore evident that informed consent symbolizes a mandatory ethical concept that is extensively implemented in law, as well as in everyday healthcare facility practice. Indeed, clinical informed consent is

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<sup>4</sup> Richa Anand Chandan Dhingra, "Consent in Dental Practice: Patient's Right to Decide," *Journal of Oral Hygiene & Health* 2(2) (2014), <https://doi.org/10.4172/2332-0702.1000129>.

<sup>5</sup> Ana Borovecki et al., "Informed Consent and Ethics Committee Approval in Laboratory Medicine," *Biochemia Medica* 28(3) (2018), [doi.org/10.11613/bm.2018.030201](https://doi.org/10.11613/bm.2018.030201).

<sup>6</sup> Prashant B. Musmade et al., "Informed Consent: Issues and Challenges," *Journal of Advanced Pharmaceutical Technology & Research* 4(3) (2013): 134, <https://doi.org/10.4103/2231-4040.116779>.

<sup>7</sup> "World Medical Association Declaration of Helsinki," *JAMA* 310(20) (2013): 2191, <https://doi.org/10.1001/jama.2013.281053>.

<sup>8</sup> C. Weijer, "Ethics: Protecting Communities in Biomedical Research," *Science* 289(5482) (2000): 1142-1144, <https://doi.org/10.1126/science.289.5482.1142>. Raul Artal and Sheldon Rubinfeld, "Ethical Issues in Research," *Best Practice & Research Clinical Obstetrics & Gynaecology* 43 (2017): 107-114, <https://doi.org/10.1016/j.bpobgyn.2016.12.006>.

<sup>9</sup> C. S. Cocanour, "Informed Consent-It's More than a Signature on a Piece of Paper," *The American Journal of Surgery* 214(6) (2017): 993-997, <https://doi.org/10.1016/j.amjsurg.2017.09.015>.

ethically, morally, and legally mandated by the fiduciary responsibilities resulting from the patient-doctor relationship.<sup>10</sup> Finally, as a form of a protective umbrella, specific research ethics committees and institutional review boards assure that participant selection protocols are unbiased, that study participation brings an acceptable ratio of benefits and harms, and that participants provided their informed consent.<sup>11</sup>

## INFORM CONSENT – THEN AND NOW

Our present comprehension of informed consent is that it represents the full disclosure of the nature of the research and the human subject's involvement, as well as an adequate understanding of the role of the prospective participant and the participant's voluntary willingness to participate.<sup>12</sup> Unfortunately, from the historical point of view, the conception of informed consent represents the valuable accomplishment of not always peaceful events in both the clinical and research settings in the not so distant past, since in fact, the notion of informed consent is the result of recognized abuses in the clinical and research fields spanning over a century.<sup>13</sup> So ultimately, in order to prevent further exploitations and unhealthy practices in the field of life sciences, the procedure of obtaining informed consent was emphasized to ensure that a human participant's rights were not in danger.<sup>14</sup>

The Nuremberg Code of conducting research on human subjects was introduced after World War II. Namely, following the conclusion of the Nazi Doctors' Trial in 1947, the justices issued the Nuremberg Code with stringent standards to be used in human experimentation, including the

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<sup>10</sup> Timothy J. Paterick et al., "Medical Informed Consent: General Considerations for Physicians," *Mayo Clinic Proceedings* 83(3) (2008): 313-319, <https://doi.org/10.4065/83.3.313>.

<sup>11</sup> Cory E. Goldstein et al., "Ethical Issues in Pragmatic Randomized Controlled Trials."

<sup>12</sup> "IRB Consent Form Templates," *IRB Consent Form Templates | Cornell Research Services*, accessed March 26, 2021, <https://researchservices.cornell.edu/forms/irb-consent-form-templates>.

<sup>13</sup> Fida K. Dankar, Marton Gergely, and Samar K. Dankar, "Informed Consent in Biomedical Research," *Computational and Structural Biotechnology Journal* 17 (2019): 463-474, <https://doi.org/10.1016/j.csbj.2019.03.010>.

<sup>14</sup> P. Arun Bhupathi and G.R. Ravi, "Comprehensive Format of Informed Consent in Research and Practice: A Tool to Uphold the Ethical and Moral Standards," *International Journal of Clinical Pediatric Dentistry* 10(1) (2017): 73-81, <https://doi.org/10.5005/jp-journals-10005-1411>.

premises that human subjects are necessary, that voluntary consent or withdrawal should be obtained, minimal research risks should be present, the research should be terminated if research subjects could be injured or harmed, the research should benefit society, the research must be based on preclinical animal studies, and most importantly, that the research subjects have the right to end participation in the study.<sup>15</sup> Later on, in 1964, the Helsinki Declaration was drafted by the World Medical Association, followed by the US Congress National Research Act of 1974, and the Belmont Report of 1979 underlining three milestone principles: 1. respect for the person; 2. beneficence; and 3. Justice.<sup>16</sup>

Owed to the fast progress in medical sciences, as well as to a variety of new information that has been accumulated, the concept of informed consent has notably changed over time.<sup>17</sup> Although the physician-patient interaction originates from the ethical concept of beneficence, over the nineteenth and twentieth centuries, the law and social changes brought respect for autonomy, too.<sup>18</sup> That way, patients have a legal, ethical and fundamental human right to choose what happens to their bodies, where the consent nowadays represents a form of the patient's agreement for a physician to provide care.<sup>19</sup> So, currently, patient autonomy and the right to choose are the paramount principles, where at the same time patient autonomy counselling has radically progressed, with the ultimate aim that patients should be the key decision-makers, but only if they are fully informed.<sup>20</sup>

Since the practice of obtaining informed consent in the research setting was designed to ensure that the participants' rights were not at risk, research subjects are now better informed and aware of their rights and alternatives, above all, their right of refusal.<sup>21</sup> Unfortunately, present

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<sup>15</sup> Evelyne Shuster, "Fifty Years Later: The Significance of the Nuremberg Code," *New England Journal of Medicine* 337(20) (1997): 1436-1440, <https://doi.org/10.1056/nejm199711133372006>.

<sup>16</sup> P. Arun Bhupathi and G.R. Ravi, "Comprehensive Format of Informed Consent in Research and Practice," 73-81.

<sup>17</sup> Fida K. Dankar, Marton Gergely, Samar K. Dankar, "Informed Consent in Biomedical Research," 463-474.

<sup>18</sup> C. S. Cocanour, "Informed Consent—It's More than a Signature on a Piece of Paper."

<sup>19</sup> Akanksha Sood and Janesh Gupta, "Patient Counselling and Consent," *Best Practice & Research Clinical Obstetrics & Gynaecology* 46 (2018): 43-47, <https://doi.org/10.1016/j.bpo.2017.10.002>.

<sup>20</sup> Akanksha Sood and Janesh Gupta, "Patient Counselling and Consent," 43-47.

<sup>21</sup> Raul Artal and Sheldon Rubenfeld, "Ethical Issues in Research," 107-114.

directives and existing laws cannot predict every reasonable ethical situation or question, particularly given the new advances in science and technology, as well as new and growing medical technology, genetic tests, pharmacological interventions, and other advances which challenge society to retain the highest moral and ethical principles.<sup>22</sup> Yet, the lack of understanding, as well as obstacles in communication, culture, custom, and different other issues, continuously demand an additional concern in obtaining valid informed consent.<sup>23</sup>

## THE COMPONENTS OF A VALID CONSENT

When it comes to the components of a valid consent, we always have to be prudent about the challenges related to the decisional capacity, information that will be provided, and the free will concerns.

### *The capacity*

First of all, it must not be presumed that a patient lacks decisional capacity for reaching a decision merely because of their age, disability, behaviour, appearance, medical condition (including mental illness), their apparent inability to communicate, their beliefs, or the fact that they make a choice that a doctor opposes.<sup>24</sup> In other words, a clinician should not doubt a patient's capacity simply because the patient's decision seems unsupported, irrational or based on a series of beliefs that are not in agreement with scientific understandings, peer-reviewed publications or the conventional social norms.<sup>25</sup>

It has to be underlined that the decisional capacity does not primarily coincide with the suitability of the final decision, but more with the pathway through which the participant arrives at that decision, given that patients have diverse capacities to understand and appreciate the information provided, as well to accept and cope with risk and

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<sup>22</sup> *Ibidem*.

<sup>23</sup> P. Arun Bhupathi and G.R. Ravi, "Comprehensive Format of Informed Consent in Research and Practice," 73-81.

<sup>24</sup> Akanksha Sood and Janesh Gupta, "Patient Counselling and Consent," 43-47.

<sup>25</sup> S. Henwood, M. A. Wilson, and I. Edwards, "The Role of Competence and Capacity in Relation to Consent for Treatment in Adult Patients," *British Dental Journal* 200(1) (2006): 18-21, <https://doi.org/10.1038/sj.bdj.4813118>.

uncertainty.<sup>26</sup> Most participants in clinical trials understand the basic elements of informed consent, such as the nature of research, possible benefits of the study, autonomy to withdraw at any time, and the voluntary nature of participation; where at the same time, the understanding of randomization or placebo was shown to be not as accurate.<sup>27</sup>

Children and patients not able to give consent must also be involved in the process, but only to the extent of their capacity to comprehend the study protocol, which indicates that where research involves participants under the age of 18, a consent/permission has to be obtained from parents, and if the child is above 7 years of age then the “child assent” is also required.<sup>28</sup>

When it comes to the frequent questions regarding the competence/capacity relationship, there is also much confusion linked to the appropriate use of these two terms. So, competence is a legal term, and all adults are presumed to be competent unless they are determined by a court to be incompetent, while capacity is task-specific, where decisional capacity is further determined by a clinician.<sup>29</sup> It needs to be emphasized that there may still be concerns in everyday practice, as to a patient’s capacity to consent to a proposed treatment, either due to their age or mental capacity.<sup>30</sup> Since capacity is task-specific, it can be divided into eight distinctive areas, detailing the abilities and skills required for each capacity.<sup>31</sup>

In determining whether a patient/participant has the decision-making capacity, the physician must determine if they are capable of these four

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<sup>26</sup> Nick Nicholas and Mohammed El Sayed, “The Changing Face of Consent: Past and Present,” *The Obstetrician & Gynaecologist* 8(1) (2006): 39-44, <https://doi.org/10.1576/toag.8.1.039.27207>.

<sup>27</sup> Nguyen Thanh Tam et al., “Participants’ Understanding of Informed Consent in Clinical Trials over Three Decades: Systematic Review and Meta-Analysis,” *Bulletin of the World Health Organization* 93(3) (2015), <https://doi.org/10.2471/blt.14.141390>.

<sup>28</sup> Prashant B. Mucmade et al., “Informed Consent: Issues and Challenges,” 134.

<sup>29</sup> Christine S. Cocanour, “Informed Consent—It’s More than a Signature on a Piece of Paper,” 993-997.

<sup>30</sup> Larner, Elizabeth and Rachel Carter, “The Issue of Consent in Medical Practice,” *British Journal of Haematology* 172(2) (2015): 300–304. <https://doi.org/10.1111/bjh.13795>.

<sup>31</sup> Jennifer Moye and Daniel C. Marson, “Assessment of Decision-Making Capacity in Older Adults: An Emerging Area of Practice and Research,” *The Journals of Gerontology: Series B* 62(1) (2007), <https://doi.org/10.1093/geronb/62.1.p3>.

abilities: understanding, expressing a choice, appreciation, and reasoning<sup>32</sup>:

1. Understanding represents the ability to know the meaning of the information, and it is a key decisional ability.
2. The second ability is whether the person can express a choice.
3. The ability of appreciation is more than just knowing the facts necessary for making a decision. It is about applying those facts to the person's own life.
4. Reasoning refers to the ability to compare options and infer the consequences of the choice.

### *Information*

The process of obtaining informed consent should be characterized by open information exchange.

The patient or study participant should be fully informed about all the risks and probable complications of the administered treatment or investigation offered, where the crucial role of the institutional review board is to ensure that the researcher makes appropriate information available to potential subjects.<sup>33</sup>

Yet, communicating specific technical and other specialized information to those with limited literacy, various social and cultural backgrounds, limited autonomy, and incapacitating diseases may be a difficult mission.<sup>34</sup> As a rule, the information should be provided in lay terms without medical jargon, since it was established that simplified information appeals to patients and is connected with reduced anxiety and increased approval rate of the consent document.<sup>35</sup>

As a useful tool for the understanding of the provided information, different techniques such as the “teach back method,” wherein research

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<sup>32</sup> Christine S. Cocanour, “Informed Consent—It's More than a Signature on a Piece of Paper,” 993-997.

<sup>33</sup> Robert J. Amdur and Elizabeth A. Bankert, *Institutional Review Board: Member Handbook* (Burlington, MA: Jones & Bartlett Learning, 2011).

<sup>34</sup> Rashmi Ashish Kadam, “Informed consent process: A step further towards making it meaningful?” *Perspectives in Clinical Research* 8 (2017): 107-112.

<sup>35</sup> Graham M. Dresden and M. Andrew Levitt, “Modifying a Standard Industry Clinical Trial Consent Form Improves Patient Information Retention as Part of the Informed Consent Process,” *Academic Emergency Medicine* 8(3) (2001): 246-252, <https://doi.org/10.1111/j.1553-2712.2001.tb01300.x>.

participants are asked to say in their own words what has been described, can be successfully employed.<sup>36</sup> Likewise, various questionnaires for testing the level of understanding can be used by introducing simple questions to be answered with<sup>37</sup>:

- yes/no,
- disagree/agree/unsure,
- short answer,
- fill-in the blanks,
- multiple-choice, etc.

The patient's understanding can also be significantly improved by using of printed brochures, particularly those enclosing a mixture of illustrations and narrative content, as well as other various information sheets offering additional information about the clinical trial.<sup>38</sup>

Nowadays, it is more than clear that the use of computers and different multimedia in the consent process may help improve the patient's understanding, given that audio-visual tools have been shown to facilitate the verbal reinforcement of written information, which contributes to the successful comprehension and recall.<sup>39</sup> In other words, the purpose of utilizing multimedia in the consent process is to translate complex study information into a comprehensible and visually appealing audio-video layout.<sup>40</sup>

The use of mobile devices, tablets and the internet for multimedia informed consent delivery is increasingly implemented in everyday routine. Still, whereas social media may boost information exchange, there is a genuine risk of ethical standards deviations, different

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<sup>36</sup> Rashmi Ashish Kadam, "Informed consent process," 107-112.

<sup>37</sup> Ibidem.

<sup>38</sup> Robert Michielutte et al., "The Use of Illustrations and Narrative Text Style to Improve Readability of a Health Education Brochure," *Journal of Cancer Education* 7(3) (1992): 251-260, <https://doi.org/10.1080/08858199209528176>.

<sup>39</sup> Loel Kim et al., "Keeping Users at the Center: Developing a Multimedia Interface for Informed Consent," *Technical Communication Quarterly* 17(3) (2008): 335-357, <https://doi.org/10.1080/10572250802100451>.

<sup>40</sup> Kathryn Blake et al., "Use of Mobile Devices and the Internet for Multimedia Informed Consent Delivery and Data Entry in a Pediatric Asthma Trial: Study Design and Rationale," *Contemporary Clinical Trials* 42 (2015): 105-118, <https://doi.org/10.1016/j.cct.2015.03.012>.

misrepresentations, and lack of validity of the information.<sup>41</sup> As an outcome of these concerns, it is strongly recommended that well before market release all novel e-consent tools and consent apps must go through stringent legal and licensing protocols.<sup>42</sup>

### *Free will*

Consent should be given voluntarily. Voluntariness implies that an individual's determination to participate is made without coercion or undue persuasion.<sup>43</sup> Indeed, the person should not be forced in any physical, financial or emotional/mental way to participate in the research.<sup>44</sup> The only person who can consent is the subject themselves.

Consent should always be obtained well ahead, rather than later, as this postponement could sometimes initiate some other delays.<sup>45</sup> At the end of the consent process, an investigator must always ask the participant if they have understood the provided information and if any additional information is necessary to facilitate the decision making process.<sup>46</sup> The physician is obliged to inform the patient of any potentially conflicting interests they may have, including financial or other research-related interests.<sup>47</sup> So, all questions should be answered as fully and honestly as possible, which also means that it is essential to emphasize during the conversation that the subject has the right to refuse to participate in the research or to withdraw from the study at any time after the beginning of the research protocol.<sup>48</sup>

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<sup>41</sup> Celia Taber et al., "Improving the Quality of Informed Consent in Clinical Research with Information Technology," *Studies in health technology and informatics* 231 (2016): 135-142.

<sup>42</sup> Roger Collier, "Apple Moves into Medical Research," *Canadian Medical Association Journal* 187(8) (2015): 559-559, <https://doi.org/10.1503/cmaj.109-5034>.

<sup>43</sup> Nguyen Thanh Tam et al., "Participants' Understanding of Informed Consent in Clinical Trials over Three Decades."

<sup>44</sup> Ana Borovecki et al., "Informed Consent and Ethics Committee Approval in Laboratory Medicine."

<sup>45</sup> O. A. Anderson and I. M. Wearne, "Informed Consent for Elective Surgery--What Is Best Practice?" *Journal of the Royal Society of Medicine* 100(2) (2007): 97-100, <https://doi.org/10.1258/jrsm.100.2.97>.

<sup>46</sup> Akanksha Sood and Janesh Gupta, "Patient Counselling and Consent," 43-47.

<sup>47</sup> "Patients' Rights and the Basic Principles of Consent," *Consent Manual*, 43<sup>rd</sup> Edition (California Hospital Association, 2016), [https://www.calhospital.org/sites/main/files/file-attachments/consent2016\\_webpreview\\_0.pdf](https://www.calhospital.org/sites/main/files/file-attachments/consent2016_webpreview_0.pdf).

<sup>48</sup> Ana Borovecki et al., "Informed Consent and Ethics Committee Approval in Laboratory Medicine."

## DIFFERENCES BETWEEN INFORMED CONSENT FOR TREATMENT AND RESEARCH PROTOCOLS

Informed consent is not only required for clinical trials, but it is a critical precondition prior to enrolment of each participant in any type of research on human subjects, including diagnostic, therapeutic, interventional, bioequivalence, social, and behavioural studies.<sup>49</sup>

### *Treatment-related consent*

Everyday clinical practice is characterized by the trust relationship between physician and patient, and informed consent obtained for the purpose of treatment is a result of a two-way conversation highlighting the physician-patient therapeutic relationship.<sup>50</sup> Indeed, today's patient-centred medicine underlines the patient's right to actively participate in the healthcare process, where we can clearly recognize a specific discussion between two equal partners (the physician and the patient) about the best possible treatment choices.<sup>51</sup>

In the everyday clinical setting, the patient is always a subject in this process, never an object, where the healthcare provider firstly establishes the patient's condition; then uses lay terms with full consideration of the patient's culture and values, and offers an opportunity for questions related to therapeutic approach and an exchange of important information.<sup>52</sup>

Since the purpose of ethics in the traditional physician-patient relationship is based on doing well, this information-sharing procedure

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<sup>49</sup> Prashant B. Musmade et al., "Informed Consent: Issues and Challenges," 134.

<sup>50</sup> B.S. Khoury and J.N. Khoury, "Consent: a Practical Guide," *Australian Dental Journal* 60(2) (2015): 138-142, <https://doi.org/10.1111/adj.12301>. Cory E. Goldstein et al., "Ethical Issues in Pragmatic Randomized Controlled Trials."

<sup>51</sup> Beth A. Ripley et al., "Improving the Informed Consent Conversation: A Standardized Checklist That Is Patient Centered, Quality Driven, and Legally Sound," *Journal of Vascular and Interventional Radiology* 26(11) (2015): 1639-1646, <https://doi.org/10.1016/j.jvir.2015.06.007>.

<sup>52</sup> Sarah Ford, Theo Schofield, and Tony Hope, "Are Patients' Decision-Making Preferences Being Met?" *Health Expectations* 6(1) (2003): 72-80, <https://doi.org/10.1046/j.1369-6513.2003.00211.x>. Cathy Charles, Amiram Gafni, and Tim Whelan, "Shared Decision-Making in the Medical Encounter: What Does It Mean? (or It Takes at Least Two to Tango)," *Social Science & Medicine* 44(5) (1997): 681-692, [https://doi.org/10.1016/s0277-9536\(96\)00221-3](https://doi.org/10.1016/s0277-9536(96)00221-3).

empowers the patient to reach the fully informed decision about accepting or declining the recommended treatment.<sup>53</sup>

However, opposite to the above considerations, there are five recognized exceptions when the informed consent of the patient is not necessary<sup>54</sup>:

- a public health emergency (for example, the use of quarantine)
- a medical emergency (the procedure is needed immediately)
- patient waiver (the patient has requested not to be informed)
- “therapeutic privilege” (a disclosure could seriously harm, rather than benefit the patient)
- in case the patient is incompetent (a need for determination of a surrogate)

### *Research-related consent*

The term *research* is traditionally linked to a class of activities designed to further contribute to general knowledge.<sup>55</sup> During this process, the investigator’s responsibility is to obtain informed consent from potential human subjects, and moreover, it has to be stressed that the research community significantly depends on the integrity of the investigator to complete the consent process successfully.<sup>56</sup>

The relationship between the researcher and the participants is guided by a specific series of rules, all with the rationale of confirming a scientific hypothesis<sup>57</sup>:

- the selection of suitable subjects
- appropriate treatment of subjects,
- careful application of research methodology,

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<sup>53</sup> B.S. Khoury and J.N. Khoury, “Consent: a Practical Guide,” 138-142.

<sup>54</sup> Christine S. Cocanour, “Informed Consent—It’s More than a Signature on a Piece of Paper,” 993-997.

<sup>55</sup> “International Ethical Guidelines for Health-Related Research Involving Humans • COUNCIL FOR INTERNATIONAL ORGANIZATIONS OF MEDICAL SCIENCES,” *COUNCIL FOR INTERNATIONAL ORGANIZATIONS OF MEDICAL SCIENCES*, October 12, 2020, <https://cioms.ch/shop/product/international-ethicalguidelines-for-health-related-research-involving-humans>.

<sup>56</sup> Robert J. Amdur and Elizabeth A. Bankert, *Institutional Review Board: Member Handbook*.

<sup>57</sup> Ana Borovecki et al., “Informed Consent and Ethics Committee Approval in Laboratory Medicine.”

- acquisition of high-quality data.

In this scenario, high ethical standards are equated with the high quality of science, which means that informed consent in research implies that participants give the researcher permission to actually treat them as an object of the research.<sup>58</sup> So one must be very careful of the so-called therapeutic misconception, which means that study participants may mistakenly believe that research activities are meant to directly benefit them and their personal health.<sup>59</sup>

The main models of informed consent with their related characteristics are presented below<sup>60</sup>:

<b>Consent model</b>	<b>Characteristics</b>
<b>Standard informed consent</b>	<ul style="list-style-type: none"><li>• Written disclosure of all information.</li><li>• Consent obtained in writing.</li></ul>
<b>Targeted consent model</b>	<ul style="list-style-type: none"><li>• Verbally disclosed information.</li><li>• Obtained written consent.</li></ul>
<b>Integrated consent model</b>	<ul style="list-style-type: none"><li>• Verbally disclosed information.</li><li>• No written consent required.</li><li>• Physician documents consent in electronic health record.</li></ul>
<b>Streamlined consent</b>	<ul style="list-style-type: none"><li>• No consent is sought.</li></ul>

Today, as opposed to some novel interpretations of informed consent, most researchers support without any doubt the notion that irrespective of the research risk levels, written record of the patient's agreement to participate in the proposed research still remains exceptionally important.<sup>61</sup> This way, we are effectively protecting a patient's decision-making role, and at the same time we are respecting

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<sup>58</sup> Ibidem.

<sup>59</sup> Cory E. Goldstein et al., "Ethical Issues in Pragmatic Randomized Controlled Trials."

<sup>60</sup> Ibidem.

<sup>61</sup> James R. Anderson, Toby L. Schonfeld, "Informed consent for comparative effectiveness trials," *The New England journal of medicine* 370(20) (2014), <https://doi.org/10.1056/NEJMc1403310#SA1>.

the person's dignity.<sup>62</sup> After all, it is assumed that an informed consent obtained in a conventional mode generates satisfaction, reduces inadequate expectations and provides documented proof of good clinical practice.<sup>63</sup>

Finally, there are some circumstances where informed consent can be waived; however, waivers of consent require justification, including the following examples:

1. the research must be socially important;
2. requiring informed consent would make the study infeasible;
3. participation poses only minimal risk.<sup>64</sup>

## DISCLOSURE OF INFORMATION

It is crucial to disclose all information about a study to the participants.<sup>65</sup> This usually includes the following items: 1. the nature of the research, 2. the purpose of the research, 3. risks and anticipated benefits, 4. any available alternative procedures, and 5. the opportunity for the subject to ask any questions.<sup>66</sup>

Specifically, the current regulations require that prospective research participants receive the following information<sup>67</sup>:

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<sup>62</sup> Ahmed Elsayyad, "Informed Consent for Comparative Effectiveness Trials," *New England Journal of Medicine* 370(20) (2014): 1958-1960, <https://doi.org/10.1056/nejmc1403310#SA3>.

<sup>63</sup> J.M. Mellado, "Autonomía, Consentimiento y Responsabilidad. Parte II. El Consentimiento Informado En La Medicina Asistencial y En La Jurisprudencia," *Radiología* 58(6) (2016): 427-434, <https://doi.org/10.1016/j.rx.2016.06.010>.

<sup>64</sup> "International Ethical Guidelines for Health-Related Research Involving Humans • COUNCIL FOR INTERNATIONAL ORGANIZATIONS OF MEDICAL SCIENCES."

<sup>65</sup> Office for Human Research Protections, "Federal Policy for the Protection of Human Subjects (Common Rule)," *HHS.gov* (US Department of Health and Human Services, March 18, 2016), <https://www.hhs.gov/ohrp/regulations-and-policy/regulations/common-rule/index.html>.

<sup>66</sup> Office for Human Research Protections, "The Belmont Report," *HHS.gov* (US Department of Health and Human Services, March 15, 2016), [www.hhs.gov/ohrp/regulations-and-policy/belmont-report](http://www.hhs.gov/ohrp/regulations-and-policy/belmont-report). Charles Weijer et al., "The Ottawa Statement on the Ethical Design and Conduct of Cluster Randomized Trials," *PLoS Medicine* 9(11) (2012), <https://doi.org/10.1371/journal.pmed.1001346>.

<sup>67</sup> Office for Human Research Protections (OHRP), "45 CFR 46," *HHS.gov* (US Department of Health and Human Services, March 10, 2021), [www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.html](http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.html).

- a statement that the study involves research;
- the explanation of its purpose and procedures;
- the description of the reasonably foreseeable risks or discomforts;
- the description of the possible benefits to the participant or society, where monetary compensation is not a benefit;
- the description of alternative treatments that might be advantageous to the subject;
- the expected duration of the study
- the explanation of the steps taken to protect the confidentiality of private health information, including a description of who may have access to research records;
- for research posing more than minimal risk, an explanation as to whether compensation will be available for research-related injury;
- explaining whom to contact about information on the research or the participant's rights;
- a statement that research participation is voluntary and study refusal (or withdrawal) will not result in the loss of benefits to which the participant has a right.

When appropriate, the following information must also be provided<sup>68</sup>:

- Unforeseeable risks: A statement that the particular treatment or procedure may involve risks to the subject (or to the embryo or fetus, if the subject is or may become pregnant) that are currently unforeseeable.
- Termination of participation by the investigator: Anticipated circumstances under which the subject's participation may be terminated by the investigator without regard to the subject's consent.
- Additional costs: Any additional costs to the subject that may result from participation in the research.
- Consequences of discontinuing research participation: The consequences of a subject's decision to withdraw from the research; and procedures for orderly termination of participation by the subject.

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<sup>68</sup> Robert J. Amdur and Elizabeth A. Bankert, *Institutional Review Board: Member Handbook*.

- Notification of significant new findings: A statement that significant new findings developed during the course of the research that may relate to the subject's willingness to continue participation will be provided to the subject.
- An approximate number of subjects: The approximate number of subjects involved in the study.

## FINAL REMARKS

Informed consent should always be considered as much more than a patient's signature on a legal document.

Informed consent must be viewed as a continuous dynamic process rather than an isolated event during the clinical study.

It is essential to adopt innovative multimedia communication strategies to further enhance comprehension of clinical trial information among participants.

Improving the usefulness and efficiency of the informed consent process is a critical healthcare and research policy issue.

Shifting the conversation from the national regulations to the internationally accepted ethical principles should be a continual process.

Developing international ethical standards for responsible conduct of clinical research trials requires the participation of all.

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