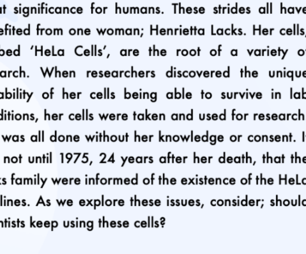
Consent Issues of Human Bodies Used for Medical Research in Modern Period

CANCER, HIV AND EBOLA RESEARCH

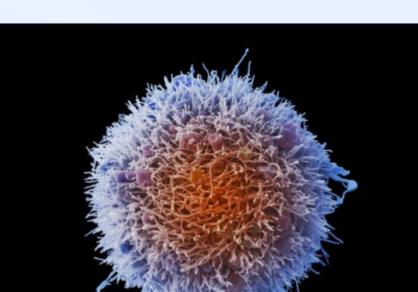
Research into cancer, HIV and the Ebola virus have had great significance for humans. These strides all have benefited from one woman; Henrietta Lacks. Her cells, dubbed 'HeLa Cells', are the root of a variety of research. When researchers discovered the unique capability of her cells being able to survive in lab conditions, her cells were taken and used for research. This was all done without her knowledge or consent. It was not until 1975, 24 years after her death, that the Lacks family were informed of the existence of the HeLa cell lines. As we explore these issues, consider; should scientists keep using these cells?



HeLa cells

Anne Weston
Date Unknown

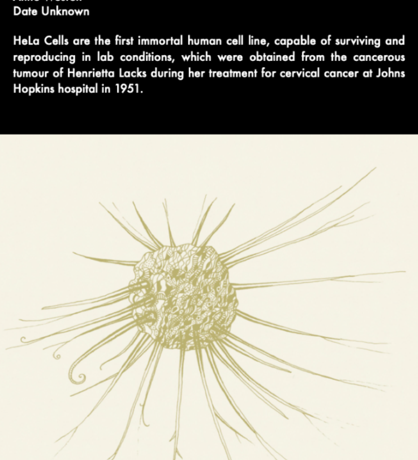
HeLa Cells are the first immortal human cell line, capable of surviving and reproducing in lab conditions, which were obtained from the cancerous tumour of Henrietta Lacks during her treatment for cervical cancer at Johns Hopkins hospital in 1951.



Cervical Cancer Cell

Kate Cragoe Mayfield
Date Unknown

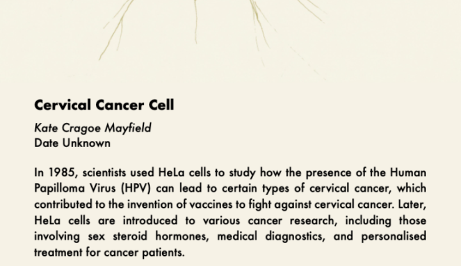
In 1985, scientists used HeLa cells to study how the presence of the Human Papilloma Virus (HPV) can lead to certain types of cervical cancer, which contributed to the invention of vaccines to fight against cervical cancer. Later, HeLa cells are introduced to various cancer research, including those involving sex steroid hormones, medical diagnostics, and personalised treatment for cancer patients.



HIV virus

London Gay Men's HIV Prevention Partnership
Date 2003?

In the 1980s, AIDS researchers used HeLa cells to understand how HIV infection works, which later facilitates the development of drugs to limit the spread of HIV.



The Ebola virus

Odra Noel
Date 2003?

In 2001, scientists using HeLa cells discovered that HIV and Ebola viruses use a similar process to enter cells and cause disease. These findings together with earlier studies on HIV, contributed to the invention of an effective Ebola vaccine.

DEVELOPMENT OF VACCINES

The invention of the vaccine has helped humans to fight against infectious diseases and has had a crucial role in the medical advancements in the 20th and 21st century. The cells from an aborted foetus of an ordinary Swedish woman, name unknown, which contributed a lot to the creation of many of the world's vaccines. The cells' name is WI-38. It was only after researchers reached out to the woman to determine if any possible family disease would affect their research that she learned of WI-38.

In the following section, we will explore the story of WI-38 cells to reveal the consent issues in obtaining them for developing vaccines and also its contributions. More importantly, we encourage you to think about in today's medical research, if it does need to involve aborted fetuses in the research, what should the researchers do to obtain the consent from their parents?

WI-38 cells (Left: in high density/ Right: in low density)

Yuanyuan Li, Trygve O. Tollefsbo
Date 2011
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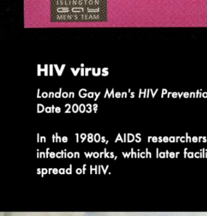
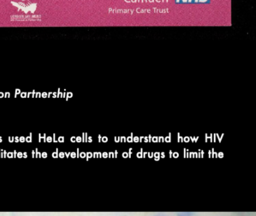
Without her consent, the aborted fetus of a Swedish women was used by the researchers at Wistar Institute in Philadelphia in 1962 to isolate cells from lungs, which aimed at providing a safe and clean environment for vaccines.





Polio vaccine

Photographer Unknown
Date Unknown

MMR vaccine, United Kingdom

Photographer Unknown
Date 1999

In the left photograph, Polio vaccine dropped on to sugar lump for child patient. In the right photograph, there is the combined MMR vaccine, which is used to protect against measles, mumps, and rubella in the United Kingdom in 1988. WI-38 cells were essential to the creation of these two vaccines, which have saved the lives of millions of people. Nowadays, it is still used to create the measles, mumps, and rubella vaccines.

REGULATIONS OF CONSENT ISSUES IN MEDICAL RESEARCH

In the 21st century, authoritative organizations in the United Kingdom set out various guidance and regulations to regulate consent issues in medical research. One example comes from the General Medical Council. Consent to Research is a guideline for researchers to understand the principles of decision making and the ways of seeking consent for various kinds of research. This guidance came into effect on the 4th May 2010.

Are these instructions in below document strict and comprehensive enough?

References to *Good medical practice* updated in March 2013

General Medical Council

Consent to research

About this guidance

In *Good medical practice*,[1] we advise doctors who are involved in research that:

- 17 You must be satisfied that you have consent or other valid authority before you carry out any examination or investigation, provide treatment or involve patients or volunteers in teaching or research.

Our guidance *Decision making and consent*[2] sets out the principles of good practice in making decisions in partnership with patients. That guidance focuses on decision making in the context of investigations and treatment, but the principles apply more widely, including to decisions on taking part in research. It gives advice on sharing information, discussing side effects, complications and other risks, and making and recording decisions. When relevant, you must follow the principles it sets out when seeking people's consent to take part in research.

This supplementary guidance is intended to explain how good practice principles in making decisions and seeking consent apply to research. It also provides advice on involving in research children or young people, vulnerable people, and people who lack capacity to consent.

Annex B explains the key elements of the legislation for seeking people's consent to take part in clinical trials of investigational medicinal products.[3]

You should read this guidance in conjunction with our other guidance, in particular:

- *Good practice in research*, which sets out the principles on which good practice in research is founded,
- *Confidentiality: good practice in handling patient information*,[4] which gives guidance on research and other secondary uses of data, and
- *0–18 years: guidance for all doctors*, which gives additional advice on research involving children or young people.

Together, these guidance documents set out the GMC's advice to doctors involved in research. You must use your judgement in applying the principles in the guidance to the types of research you undertake, and to the situations you face in practice as a doctor, whether or not you hold a licence to practise. You must be prepared to explain and justify your decisions and actions. Only serious or persistent failure to follow our guidance that poses a risk to patient safety or public trust in doctors will put your registration at risk.

Seeking consent

Valid consent

1 Seeking consent is fundamental in research involving people. Participants' consent is legally valid and professionally acceptable only if they have the capacity to decide whether to take part in the research, have been properly informed, and have agreed to participate without pressure or coercion.

2 When conducting research involving people who cannot consent for themselves, you must follow the guidance that applies, such as the advice on research involving children or young people in paragraphs 14–20 and on adults who lack capacity in paragraphs 23–35.

Right to withdraw from research

3 You must make sure that people are informed of, and that you respect, their right to decline to take part in research and to withdraw from the research project at any time, with an assurance that this will not adversely affect their relationship with those providing care or the care they receive. You should tell people if the treatment options available to them might be affected by a decision to withdraw from a research project.

Sharing information

4 You must give people the information they want or need in order to decide whether to take part in research. How much information you share with them will depend on their individual circumstances. You must not make assumptions about the information a person might want or need, or their knowledge and understanding of the proposed research project.

5 In most cases, the information people will need to decide whether to take part in research will be included in the participant information sheet. The National Research Ethics Service gives advice on the design of information sheets and consent forms, and the key points they should cover. You should follow that advice if you are developing information sheets or consent forms.[5]

6 You should give people any further information they ask for. This might include a copy of the protocol approved by a research ethics committee (subject to considerations of confidentiality, commercial privilege or the possible undermining of the purpose of the study). You should make sure people have the details of an individual or organisation they can contact to discuss the research project and get further information.

Giving information in a way that people can understand

7 You must make sure that people are given information in a way that they can understand. You should check that people understand the terms that you use and any explanation given about the proposed research method. If necessary, you should support your discussions with simple and accurate written material or visual or other aids.

8 You must make sure, wherever practical, that arrangements are made to meet people's language, communication and other support needs. It is important to make sure that people who require additional assistance are not excluded from research and from the benefits that research can offer them and the wider groups to which they belong.

Responsibility for seeking consent

9 If you are responsible for seeking consent, you must understand the research project, including what the project will involve and any anticipated benefits and foreseeable risks.

10 If you delegate the responsibility to someone else, you must make sure they have sufficient understanding of the research project, and the appropriate skills and competence to seek consent.

Recording consent

11 You should record the key elements of your discussion with people about their decision to take part in research. If practical, you should ask them, or someone with valid authority, to give written consent. It is a legal requirement to get written consent from participants in clinical trials of investigational medicinal products.[6]

Sharing information with others involved in care

12 With the participant's consent, you should usually inform their GP and other clinicians responsible for their care about their involvement in a research project, and you should provide the doctors with any other information necessary for the participant's continuing care. You should follow this advice regardless of whether the participant is a patient or a healthy volunteer.

13 If a participant objects to information being shared in this way, you should explain to them the potential consequences of not sharing information. If the participant continues to object, you must respect their wishes, unless sharing the information is justified in the public interest.[7]

Areas requiring special consideration

Research involving children or young people

14 When considering involving children or young people in research, you must follow the advice in *0–18 years: guidance for all doctors*.[8] It gives advice on the circumstances in which children or young people can be involved in research, effective communication with children and young people, and assessing capacity to consent. It also explains the different legal requirements across the UK for 16 and 17-year olds who lack capacity to consent.

15 There are particular considerations in relation to seeking and acting on consent for children or young people to participate in research. As part of seeking approval for the project from a research ethics committee, you must clearly explain the arrangements for getting consent and seek advice if necessary.

16 Before involving a child or young person in research you must get consent from a parent,[9] but you should get consent from both parents, if possible, particularly if the research involves more than low or minimal risk of harm. If a parent is under 16 years of age, you must get consent from them if they have the capacity to make a decision about whether their child should take part in the research project. If a child or young person is able to consent for themselves, you should still consider involving their parents, depending on the nature of the research.

17 You should aim to reach a consensus with parents about a child or young person's participation in research. If disagreements arise it is usually possible to resolve them informally, and you should follow the advice in paragraphs 92–93 *Decision making and consent*. If disagreements cannot be resolved informally, you should not involve the child or young person in research, unless the treatment can be accessed only as part of a research project and you assess that it is in their best interests. In these circumstances, if the decision about entering the child or young person in research has significant consequences for the child or young person, you should seek legal advice about whether you should apply to the appropriate court for an independent ruling.

18 You should be familiar with the guidance on involving children or young people in research published by other relevant organisations,[10] for example, the Medical Research Council, the Royal College of Paediatrics and Child Health, the Royal College of Physicians of London, and the British Medical Association.

Annex B contains specific advice on some of the legal requirements for involving children or young people under 16 in clinical trials of investigational medicinal products.

Emergency research

19 Circumstances may arise where involvement in research has the potential to benefit a child or young person who lacks capacity, but an urgent decision about the child's involvement needs to be made before it is possible to get consent from a parent. This may arise because a parent cannot reasonably be contacted, or they do not have capacity to consent because of their own condition or distress. In such cases you can involve a child or young person in research if you have the approval of a research ethics committee for such recruitment. You must seek the consent of a parent as soon as possible to continue involving them in the project.

20 There are specific legal requirements that relate to involving children or young people under 16 in emergency clinical trials of investigational medicinal products. Annex B contains further guidance on the legal requirements in these circumstances.

Research involving vulnerable adults

21 Some adults with capacity may be vulnerable to pressure to take part in research. You should be aware that their health or social circumstances might make them vulnerable to pressure from others. Vulnerable adults may be, for example, living in care homes or other institutions, or have learning difficulties or mental illness. In these circumstances, it is particularly important that you check whether they need any additional support to understand information or to make a decision.[11] You must make sure that they know they have the right to decline to participate in research, and that they are able to decline if they want to. The Royal College of Physicians of London provides further guidance on involving vulnerable groups in research.[12]

22 You should raise concerns with a senior colleague, or your employing or contracting organisation, if systems are not in place to provide the additional support that vulnerable adults may need to make a decision about taking part in research. If you are not sure when or how to raise concerns, you should follow the guidance in Raising concerns about patient safety.[13]

Research involving adults without capacity

23 This section gives guidance about specific issues in research involving adults who lack capacity. It sets out the key elements of the law that governs the involvement of people over 16 who lack capacity to consent. Annex A contains a summary of the law in this area, and annex B explains the key elements of the legislation that governs clinical trials of investigational medicinal products in the UK.

24 You must assess an adult's capacity to make a particular decision at the time it needs to be made. You must follow the guidance in paragraphs 76, 78, 79 and 84–86 of *Decision making and consent*,[14] which gives advice on maximising a person's ability to make decisions, and on assessing capacity.

When adults without capacity might be involved in research

25 You must only undertake research involving an adult who lacks capacity if it is related to their incapacity or its treatment. You must not involve in research adults who lack capacity if the same or similar research could be undertaken by involving only people with capacity.

26 You should only involve in research adults who lack capacity, including clinical trials of investigational medicinal products, if the research is expected to provide a benefit to them that outweighs the risks. Research, not including clinical trials of investigational medicinal products, may also involve adults who lack capacity if the research is not expected to provide a direct benefit to them but is expected

to contribute to the understanding of their incapacity, leading to an indirect benefit to them or others with the same incapacity, and if the risks are minimal. This means that the person should not suffer harm or distress by taking part. In all research involving adults who lack capacity, you must make sure that the foreseeable risks are kept as low as possible.[15]

Seeking to involve adults without capacity in research

27 You should consider the views of people close to the adult who lacks capacity to consent before involving that person in a research project. They are often best placed to know the person's wishes about taking part in research. In clinical trials of investigational medicinal products, you must get consent from a legal representative.[16]

28 Under the *Mental Capacity Act 2005* (in England and Wales) you must consult a consultee[17] about whether the adult who lacks capacity should take part in the research, and what they think that person's wishes would be if they had capacity to decide for themselves. If the consultee considers that they probably would not wish to take part, you must not include them in the research. Under the *Adults with Incapacity (Scotland) Act 2000*, you must get consent from any guardian or welfare attorney who has power to consent to the adult's participation in research or, if there is no such guardian or welfare attorney, from the person's nearest relative.[18]

29 If you are seeking to involve an adult who has lost capacity to consent, for example, through onset or progress of a condition that has impaired their capacity, such as dementia, you should take all reasonable steps to find out whether they have previously indicated their wishes about participating in future research, including any refusal to participate. You must consider any evidence of the person's previously expressed preferences, such as an advance statement or decision.[19]

Right to withdraw from research

30 You must make sure that a participant's right to withdraw from research is respected. You should consider any sign of objection, distress or indication of refusal, whether or not it is spoken, as implied refusal. Under the *Mental Capacity Act 2005* (in England and Wales) you should usually withdraw the participant from the research if the consultee considers that they would wish to be withdrawn. In clinical trials of investigational medicinal products, the legal representative can withdraw the participant from the trial at any time.

Loss of capacity during a research project

31 Some people with capacity will consent to take part in research, but then may lose capacity before the end of the project. If you become aware that a participant has lost capacity, you should consider carefully the benefits and harm that could occur from their continued participation in the research, and you must follow the law that applies where you work.[20]

32 If you are seeking to involve a person in research who you believe may lose capacity during the course of the project, you should consider seeking their views about the circumstances in which they would wish to continue to participate. You should explain to them the steps that would be taken to decide whether they should continue to take part and how their wishes, if known, would be taken into account.

Research into treatment in emergencies

33 You may want to undertake urgent research into procedures or treatments used in emergencies when a person is unconscious or otherwise unable to make a decision. In an emergency situation it is not always possible to get consent to involve a person in research using the standard consent procedures.

34 The *Mental Capacity Act 2005* permits urgent research in emergencies to start when it is not practical to consult someone about involving a person who lacks capacity in research. In this

situation you must either get agreement from a doctor not involved in the research, or follow a procedure approved by a research ethics committee. Similarly, you can start a clinical trial of investigational medicinal products when it needs to be undertaken urgently if you cannot get the consent of a legal representative, as long as a research ethics committee has given approval for such action. The *Adults with Incapacity (Scotland) Act 2000* provides for emergency clinical trials of investigational medicinal products but not for other types of emergency research. If this situation arises you should seek legal advice on how to proceed.

35 You must follow the law on continuing to involve in emergency research an adult who lacks capacity. You must get consent from the adult as soon as possible if they recover capacity.

Research involving human tissue

36 You must keep up to date with, and comply with, the laws and codes of practice that apply to the use in research of human organs, tissue and cells. The Human Tissue Authority (HTA) publishes a number of codes of practice,[21] including those on consent and research, which advise on the issues you should consider when seeking consent for the purpose of research.

37 In England, Wales and Northern Ireland, the *Human Tissue Act 2004* requires consent[22] to be obtained before the storage and use of a living person's organs, tissue or cells for the purpose of research in connection with disorders in, or the functioning of, the human body. In a number of specific circumstances, there are exceptions to the consent requirements; for example, a living person's organs, tissue or cells may be stored and used without consent if the researcher is unable to identify the person it has come from, and if it is used for a specific research project that has been approved by a research ethics committee. The *Human Tissue Act 2004* also requires consent to be obtained for the removal, storage and use of a deceased person's organs, tissue and cells for the purpose of research in connection with disorders in, or the functioning of, the human body. Regulations[23] made under the *Human Tissue Act 2004* permit the use and storage of organs, tissue or cells from adults who lack capacity for research under certain circumstances.

38 The *Human Tissue (Scotland) Act 2006* requires authorisation to be obtained before the storage and use of a deceased person's organs, tissue or cells for the purposes of research.[24] The Act does not cover the storage and use of tissue from living people for the purposes of research.

39 The *Medicines for Human Use (Clinical Trials) Regulations 2004* apply to the use of tissue in clinical trials of investigational medicinal products.

Endnotes

1 Good medical practice (2013).

2 *Decision making and consent*

3 Under the *Medicines for Human Use (Clinical Trials) Regulations 2004* a clinical trial means 'any investigation in human subjects, other than a non-interventional trial, intended –

a to discover or verify the clinical, pharmacological or other pharmacodynamic effects of one or more medicinal products,

b to identify any adverse reactions to one or more such products, or

c to study absorption, distribution, metabolism and excretion of one or more such products, with the object of ascertaining the safety or efficacy of those products'.

An investigational medicinal product 'means a pharmaceutical form of an active substance or placebo being tested, or to be tested, or used, or to be used, as a reference in a clinical trial, and includes a medicinal product which has a marketing authorisation but is, for the purposes of the trial -

a used or assembled (formulated or packaged) in a way different from the form of the product authorised under the authorisation,

b used for an indication not included in the summary of product characteristics under the authorisation for that product, or

c used to gain further information about the form of that product as authorised under the authorization'.

4 *Confidentiality: good practice in handling patient information.*

5 Information & consent forms. Guidance for researchers and reviewers (pdf) (National Research Ethics Service, 2011).

6 In clinical trials of investigational medicinal products, consent is only valid if it is recorded in writing. If the person is unable to give written consent, for example, if they have a disability which means that they cannot write, they can give consent orally in the presence of at least one witness and this must be recorded in writing.

7 Paragraphs 26–33 of *Confidentiality: good practice in handling patient information* provide further advice on sharing information with others involved in care.

8 *0–18 years: guidance for all doctors.*

9 References to parent or parents in this guidance mean those with parental responsibility for the child. See appendix 2 of 0-18 years: guidance for all doctors for an explanation of this term. You should also consider the views of others who are close to the child or young person but who do not have parental responsibility.

10 *Medical research involving children* (pdf) (Medical Research Council, 2004), *Guidelines for the ethical conduct of medical research involving children* (Royal College of Paediatrics and Child Health: Ethics Advisory Committee, 2000), *Guidelines on the practice of ethics committees in medical research with human participants* (Royal College of Physicians, 2007).

11 Paragraphs 11, 13b, 21, 27–29 of *Decision making and consent* provide guidance on sharing information.

12 *Guidelines on the practice of ethics committees in medical research with human participants* (Royal College of Physicians, 2007).

13 *Raising concerns about patient safety.*

14 *Decision making and consent.*

15 For the legal requirements to involve an adult without capacity in research see the *Mental Capacity Act 2005* (section 31) and the *Mental Capacity Act 2005* Code of Practice (chapter 11, paragraphs 11.9-11.19); *Adults with Incapacity (Scotland) Act 2000* (section 51); *Medicines for Human Use (Clinical Trials) Regulations 2004* (schedule 1, part 5).

16 A legal representative under the *Medicines and Human Use (Clinical Trials) Regulations* 2004 means a person who is suitable to act as a legal representative for a minor (under 16) or an adult who lacks capacity for the purpose of the trial and is available and willing to do so. They must not be involved in the conduct of the trial. For trials involving adults who lack capacity in Scotland, a legal representative means any guardian or welfare attorney who has power to consent, or the adult's nearest relative. In all cases, if there is no such person, a doctor not connected with the conduct of the trial but who is responsible for the medical treatment of the minor or adult, or a person nominated by the relevant healthcare provider can be approached. You should refer to the regulations for a full description.

17 *Guidance on nominating a consultee for research involving adults who lack capacity to consent* (Department of Health, 2008).

18 *The Adults with Incapacity (Scotland) Act 2000 Part 5 Code of Practice: A short guidance to the Act* provides information about guardian and welfare attorneys.

19 *Mental Capacity Act Code of Practice* (chapter 11, paragraph 11.30); *Adults with Incapacity (Scotland) Act 2000 Part 5 Code of Practice* (the general principles section); *Medicines for Human Use (Clinical Trials) Regulations 2004* (schedule 1, part 1, section 1(5)).

20 There are specific regulations under the *Mental Capacity Act 2005* for participants who gave consent before 31 March 2008 to take part in research that began before October 2007 but subsequently lost capacity to consent to continue to take part in the project.

Mental Capacity Act 2005 (Loss of Capacity during Research Project) (England) Regulations 2007.

Mental Capacity Act 2005 (Loss of Capacity during Research Project) (Wales) Regulations 2007.

There are no specific legal provisions under the *Adults with Incapacity (Scotland) Act 2000* relating to the loss of capacity during research in Scotland.

In clinical trials of investigational medicinal products, consent from an adult to participate in a trial remains valid after loss of capacity providing the trial is not significantly altered (*Medical Research Council ethics guide: medical research involving adults who cannot consent, 2007*).

21 *Human Tissue Authority - Codes of Practice*

22 *The Human Tissue Authority's Code of Practice* 9 – Research advises that you can rely on generic consent but you must make sure consent is valid. If the intention is to store the tissue for an as yet unknown research purpose or as part of a tissue bank for research then this should be explained, setting out the types of research that may be involved, any wider implications and the circumstances under which the tissue will be disposed of.

23 *Human Tissue Act 2004 (Persons who Lack Capacity to Consent and Transplants) Regulations 2006.*

24 *Summary of legal requirements for research with human tissue in Scotland* (pdf) (Medical Research Council, 2007)

Code: GMC/GPiRCR/1120

Consent to Research

General Medical Council
Date 2010

The **Human Tissue Act 2004** provides the framework for the regulation of human tissue research in England, Wales, and Northern Ireland. Scotland has its own **Human Tissue (Scotland) Act 2006**. Other than clinical trials of investigational medicinal products, any medical research involving people over 16 who lack capacity is governed in England and Wales by the **Mental Capacity Act 2005** and in Scotland by the **Adults with Incapacity (Scotland) Act 2000.**

Where we are now

In this whole section, we tell the stories of HeLa cells and WI-38 cells and introduce one of the guidance relating to consent issues in medical research. We understand that you may have different values, culture background and religious belief, so we encourage you to find your own ideas on each of them.

From the past to the present, the magnitude of these issues of consent becomes clearer and more concerning to our lives. Though currently, we have regulations and legislations to avoid those issues, it begs to wonder if they are the best solution. Now, let's move on to the future, where we may find new possibilities to avoid consent issues in the medical research.