**Health Research Fundamentals**
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**Lecture - 19**
**Ethical framework for health research**

Hello, in this course of Health Research Fundamentals, today we are going to talk about and discuss about some of the ethical issues in health and biomedical research. It is important that, we as researchers know what these issues are and how to protect the welfare and safety of the research participants that are going to be as a part of our research.

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It is always important to remember that ethical foundation is considered as implicit for conducting any kind of research and it is applicable not only to health research, but to any research in general. There are certain international guidelines that have been set in, there are certain international standards and we have to be within those standards. But we also have to remember that, there are Indian national standards that are available, which have been developed by Indian Council of Medical Research and they are not at all less exacting and we have to follow these guidelines as well.

Ethics review is expected in situations sometimes there is a feeling that ethics review is important only in cases where there is a significant risk involved, some invasive

procedures involved, but that is not true. Even when we are using available data, where we say that there is no risk involved to human participants, ethics review is required. Also, there are sometimes some situations when minimum risk is involved say like only questions are asked to people were no samples and specimens are collected. Even in these situations ethics review is considered important and mandatory.

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In the past so many decades, many international documents have been developed and that have helped for improving the practice of ethics in biomedical research. This all started with some kind of experimentation that was done in the World War II, among the captives and after that whatever happened, the people felt that lot of atrocities got committed and human subjects where used for research in an improper way and lot of discussions started on that. One effort in this direction which began very early was the development of the Nuremberg Code in 1947, which started some discussion related to the rational and justification of research, basically whether that particular research is necessary? What is the risk benefit analysis? How it is important in deciding whether that particular research is important or not? Also, looking at the competence of investigators and also initiated some discussion on the voluntary consent in any kind of research.

Thereafter, for the first time many countries came together and met and they signed on a document, what is called as Helsinki Declaration in 1964, which got revised several times after that and the latest revision came up in 2013. Helsinki Declaration, basically

talks about commitment to individual rights to make informed decisions, but at the same time also emphasizes duties of investigators. Also, talks about patients rights, research participants welfare and in addition talks about certain groups that are considered as vulnerable and it is necessary that certain steps are taken to protect their interest.

In the United States, in 78-79 Belmont report was published, which described the basic ethics principles of autonomy, justice and beneficence and we are going to cover this during this particular session a little later. And it also reemphasized the importance of informed consent in research and here was for the first time the importance of review by ethics committees, which are called as Institutional Review Board in the west, it was emphasized. Again in 1992-93, the Council of International Organization on Medical Sciences and WHO called CIOMS, they developed the document called as CIOMS guidelines and which was revised in 2002. This is another important international document, which provides guidelines regarding reporting of adverse events and safety of research participants. This is particularly significant in case of clinical research and clinical trials, where experimentation is done, in case of new drugs and new vaccines and so on.

It also talked about benefit and risk balance and need and principles of pharmacovigilance. So, it was stressed for the first time that by doing phase 1, 2 and 3 studies our responsibility does not end, but probably we need to do a continued surveillance in the population to figure out, what is happening on as far as the long term safety of these interventions are concerned.

In 1996, the International Council on Harmonization, ICH as it is popularly called as developed basic guidelines for good clinical practice. Subsequently, taking the basic clues from this particular document, good clinical laboratory practice document has been developed; good clinical epidemiological practice, a document has been developed. So, it found lot of applications in different spheres of health related research.

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India was not far behind in developing its own documents. The Indian Council of Medical Research in 2000 for the first time introduced Ethical Guidelines for Research on Human Participants. This was a major consensus document, which was produced and got revised in 2006 and is again in the process of revision, which might happen in the next year that is 2016. This document is available on the website of Indian Council of Medical Research. Basically, it gives the guidance for all the institutions in the country, which carry out any kind of biomedical or health research, which involves human beings and provides the guidelines that people have to follow, the researchers have to follow to protect the safety and well being of all individuals.

But in addition to that there are several other national guidelines, which are also available which include the document on genome policy and genetic research. There has been an amendment to Drugs and Cosmetic Act in the early 2000, which is available. There are guidelines available for stem cell research, assisted reproductive technologies, bio banking and researchers working in these areas have to be aware of the guidelines, which have been provided and stick to those.

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I earlier mentioned that there are certain important basic ethical principles. Among them respect for autonomy, justice, beneficence and non-maleficence, these are the ones, which have to be considered. Autonomy is considered as basically is a Latin word for self-rule, which means we have to respect individuals for what they are and this is like respecting human dignity and so we must not interfere in what people feel like doing or what peoples thought processes are. But at the same time also indicates that all those people who are not adequately aware have to be empowered to understand, what this is all about as well. Basically, what it means is people should be clearly informed that they have a right to decide to participate in research or not to participate in research.

The next principle, which is of justice, it emphasizes that we have an obligation to provide all with whatever they deserve. Basically, what it means is the participants or if there is an obligation to treat all people equally, fairly and impartially. So here, what is required is the benefit of research should be extended to everybody and except in certain situations there are certain groups like say, for example, condition like pregnancy, when women cannot participate in research. So, unless contraindicated, all groups should have an opportunity to participate in research, but this should never be imposed on anybody.

The next two principles, like they just go hand in hand. Beneficence means we must do everything which is fair and which is correct and we should be correct in our actions and in our deeds also and we should take only positive steps to prevent any kind of harm, this

is an important thing. Non-maleficence is the other side of it, we must do everything to do things to help people, we should also not cause any harm to others. So, do no harm is the principle or the explanation of what we called by non-maleficence. So, whenever harm is evident, see whenever we talk about any new drug trial for example, there is always expectation that some kind of a side effect would always be there. What we have to really ensure as researchers is that we take appropriate steps to ensure that this harm would be minimum and if at all it occurs appropriate care is taken care of. So, whenever we conduct any kind of a research, we have to ensure that these basic ethic principles or ethical principles are followed.

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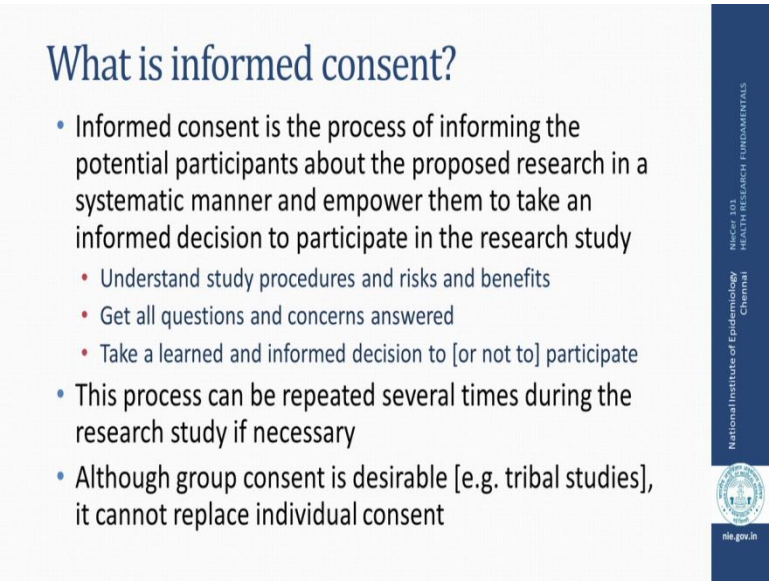


And one way to assure this is through a process is what is called as informed consent. This is a process as I very specifically mentioned because sometimes it is not a onetime event, it is not a tick mark. It is a very systematic way in which the proposed research is explained to the potential participants in a systematic step by step process and the potential participants are empowered to take an informed decision to participate in the research study. What does it involve actually? So, that the participants have to understand, what the study procedures are and what are the risks and benefits of their participation? They can ask, they can have the liberty to ask all kinds of questions and raise their concerns which have to be appropriately answered and then finally, the participants take a very appropriate learned and informed decision to participate or not to participate in the study.

So, there could be several sessions that could be involved in completing this process. A certain individual may understand the whole process in one single sitting. For an individual, it may require multiple sittings and multiple sessions, but the researchers have to be persistent and perseverant to take the potential participants through this process meticulously. In certain situations, like when we work in a certain tribal populations, institutional setups, it is important to take a group consent or consent from the concerned authorities, but one has to remember that this kind of a consent does not replace the individual consent.

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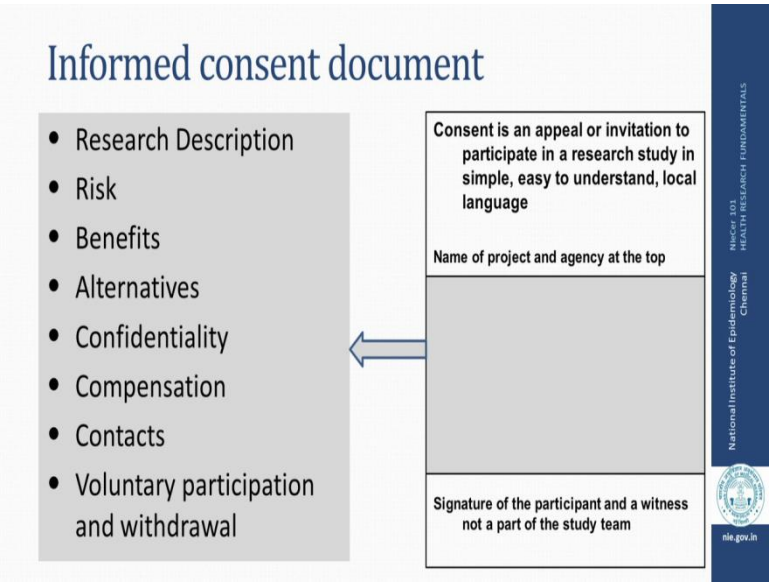


The informed consent, it is classically a document, which explains various things and so the document has at its header, the name of the project and the agency that is conducting this particular research and the main body of this particular document talks about various things like, it describes the research study in brief, it talks about the potential risks, it talks about the benefits. Sometimes, it is possible that when research is conducted, benefits are not necessarily individual oriented. The research might cause benefit to the whole community and that has to be explained correctly. Their alternatives have to be explained in the sense that participants have to be explained that, even if they decide not to participate in research, it is just fine and they will continue to get the services as they would otherwise get even if they decide not to participate.

In addition, the researchers have to commit and give the assurance of confidentiality,

keeping their records confidential because sometimes some sensitive information gets collected and participants may be worried about the information that their sharing with the research team and so it is important that they have to be given this assurance of confidentiality. Sometimes, some harm that results as a part of research participation has to be appropriately compensated and that clause also is essential as a part of the informed consent processes. We have to also give some basic important contact information as to whom the research participants can contact for any additional information, for any concerns that they may have during participation of the study and this information should be clearly included.

In addition, one of the most important clauses that gets added is about voluntary participation. The document has to emphasize that the every person has a right to decide whether to participate in the research study or not. Also, during the part of the research study and this becomes particularly important when it is a long term follow up study. A person may decide to drop out of the study at a certain point of time and it is perfectly within the rights of the individual to do so and this has to be explained. So, all these constitute the body of the informed consent and towards the end of this particular form, the signature of participant and if the participant is illiterate, then the signature of a witness who is not a part of the study team has to be obtained.

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There are various stakeholders in this informed consent process. In research, please

understand that this informed consent procedure is considered as a very important procedure and it is a very sacrosanct procedure. We as researchers have to understand that we and our institutions have an obligation to provide the required information, which is good in length and also in-depth to the participants. They should be given a chance to discuss their issues, their problems. They should be provided with adequate explanation. We have to also ensure that they have understood the information that is being given to them with respect to the research study appropriately and then also ensure that they take a voluntary decision; there is no coercion or coaxing on part of the researchers.

On part of the participants, who are the other kinds of stakeholders in this whole process, they have to themselves ensure that, they have understood whatever has been told to them. They just should not sign the informed consent form without understanding what goes behind that or what is included under that. They have to understand their rights, they have to understand various provisions, the researchers or scientists are going to make as a part of the informed consent document. Basically, they should sign the form freely, independently and without any coercion or force.

The third kind of stakeholders in this process includes the sponsors, the monitors or regulators here. These are the kind of agencies that assess the fairness of the consenting processes at various levels. This starts right from the beginning of the research study before it gets approved by the institutional ethics committee right up to monitoring throughout the procedure by the monitors and regulators as well. They also have an authority to verify the consent documentation of research participants. So, every person who is involved in research has a combined responsibility to ensure that informed consent is appropriately taken.

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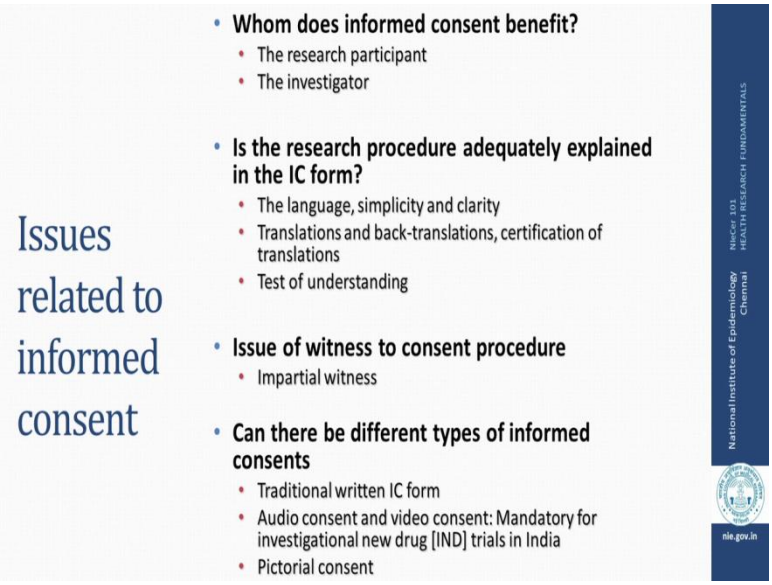


There are certain issues around that, whom does the informed consent benefit? It benefits everybody really; I talked about some stakeholders here. So, from the research participant point of view, it gives him lot of information and it therefore it is important for him, for the investigator it is a documentation that this particular process has been completed in the best possible way in the most appropriate way.

What is important to understand is whether the research procedure and various other aspects of research are adequately explained in the informed consent form. So, the language has to be simple. There has to be lot of clarity on various issues, it should be in the local language. So, it is also advised that the consent form which is developed in the local language is back translated and then either it is certified or checked with the original English consent form for its accuracy. Some investigators have tried doing test of understanding also and this is considered as one of the good practices. Once, the informed consent form is done, some kind of a small objective type of test is quickly given to the research participants to assess, whether the understanding on the informed consent form has been adequate or not.

The issue of witness can become a critical issue. This becomes particular important in scenarios, where the people are not literate and they cannot sign the informed consent form. So, here is where, there is a need to have an impartial witness. It is important to ensure that the principal investigator, researcher himself does not sign as the impartial

witness. It should be somebody, who is not connected with the research process.

There has been a lot, which has been talked about, whether the oral consent is valid or not. Typically, there should be two informed consent forms to be signed and then one has to be returned back to the participant, which the participant can keep with him for record because it also provides lot of answers to the questions that might arise in the mind of the participant subsequently. There has been some discussion going on with respect to audio consent and video consent, well the regulatory authorities in India have now made it mandatory to record the consent procedures in case of investigation in new drugs in India. So, this is an important regulation which we must keep in mind.

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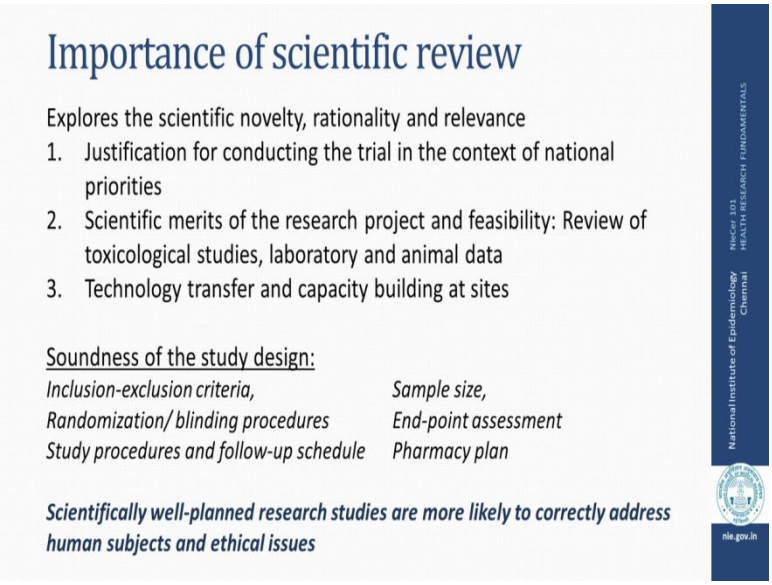


Different types of reviews have to take place before any kind of study becomes ready to be undertaken there actually. There is a scientific review and regulatory review, which takes place before the actual ethics review happens. The scientific review looks at the novelty, the rationality and relevance of the study. Basically, what is the justification of doing this particular study? What are the scientific merits? Whether appropriate study procedures have been done, have been taken into consideration? What are the inclusion exclusion criteria? Whether the sample size has been calculated appropriately? How will the endpoint or the outcomes going to be assessed? So, these aspects are normally looked at in the scientific review. Why this is important is because scientifically well planned research studies are often likely to be correctly addressing the human subject issues and

also the ethical issues. So, if the science is good often it takes care of ethics which is behind that.

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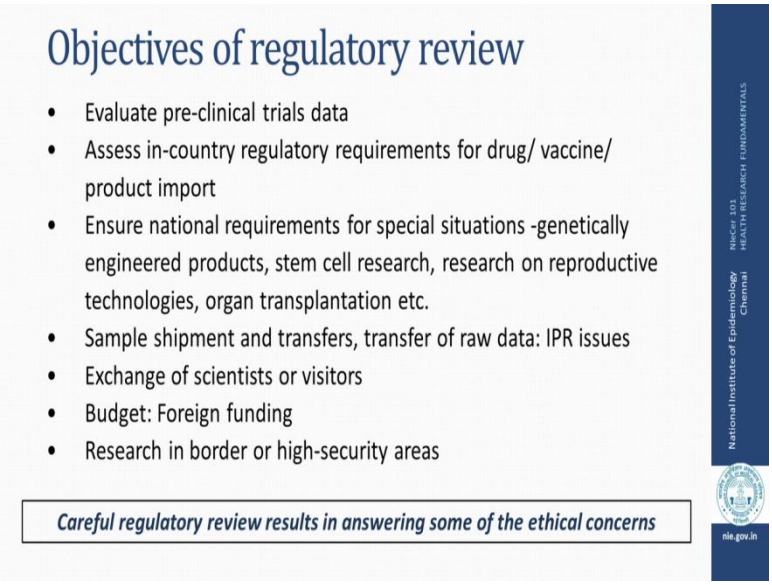


Similarly, regulatory reviews look at the various aspects like the pre-clinical trials data that has been done. This is particularly important in case of newer drugs, newer vaccines, various animal data that is there, toxicology data that is there. then there are certain in country regulatory assessments for various drug vaccine or product imports, they have to be assessed and this is important if there are certain trials or experiments which are being done using the products that have been developed abroad. There could be certain special situations, where genetically engineered products are being used or there is a stem cell research, research on the reproductive technology, organ transplantation etcetera and so the concerned regulatory agencies have to ensure that all the necessary guidelines have been followed here.

The issues around sample shipment and transfer as well as transfer of raw data is looked at very seriously by the Government of India because there are issues around the intellectual property rights in this area and the government is very protective about those. So one, the researchers have to know these issues fairly well and the regulation in this regard as well. There are certain sort of caveats; there are certain kind of restrictions regarding exchange of scientists and visitors. The funding particularly, if there is foreign funding coming in for a project to be done in India and during such situations, where the

research is to be done in the border or high security areas and the researchers have to be aware of the regulatory requirements in such situations. Again, like scientific review, careful regulatory review also results in answering some of the ethical concerns.

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Now, coming to the various ethical issues that need to be addressed; well, it is important that the competence of researchers and a research team has to be accessed appropriately. Then whatever are the provisions made for protection of human rights and vulnerable populations, in particular they have to be accessed. Then measures for protecting confidentiality, they have to be seen. Appropriateness of the informed consent form, the correct completeness of the informed consent form has to be assessed. Mechanism for reporting and management of adverse events and serious adverse events, this is particularly important in case of drug trials. Then care and support mechanism for participants, is the support going to be extended to the participants after the trial? Will the post trial benefits be given to the community after the trial is finished and is proved to be useful? These aspects also have to be looked at from the ethical angle.

The reimbursements and compensation are important issues, which the ethics review looks at. Because one has to ensure that reimbursement is for the time lost and also the expenses paid for traveling to the clinical research site. But the compensation or the incentive given or the money that is given should not be as much as to course the participant to participate in the research trial. So, this decision is also made by the ethics

committee. And it is also important to continue the review of the progress of the study till it is completed. So, the committee which really looks at all these things is what is called as Institutional Ethics Committee in India.

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It is called as Institutional Review Board abroad. Basically, it looks at whether the study has potential benefits or community benefits? Whether the rights of the participants are adequately protected? Whether the benefits of this particular study out with the risks that are involved here? Whether the participants and communities have access to study findings? Whether they are eventually going to benefit from the research participation? And what kinds of mechanisms are built-in to provide the safety and care and support to research participations even during the study and after the study?

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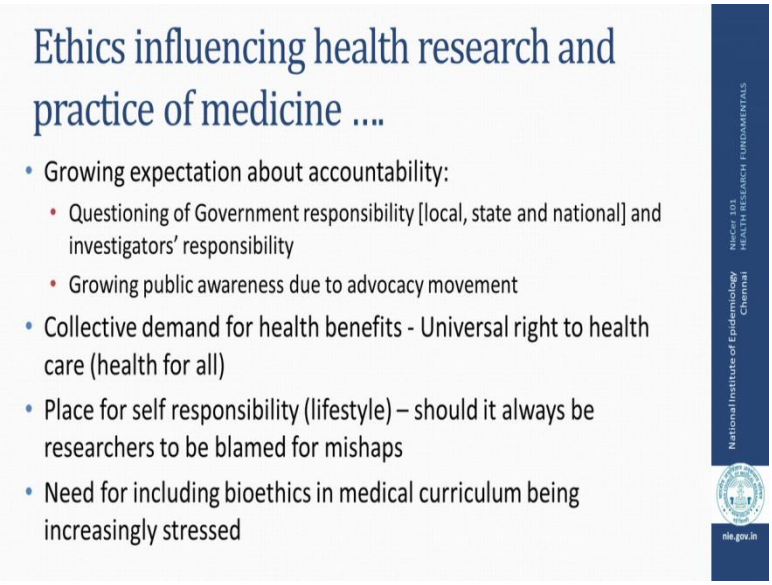


So, there are growing expectations about accountability from the researchers now. Various researchers are being questioned about their responsibility and governments' responsibility as well in fairly conducting research. There is a growing public awareness also; all this is eventually going to improve the quality of research in our country and also, the practice of medicine in our country over a period of time. There is a collective demand for health benefits, people are demanding. So, universal right to health care which emanates from the principal of health for all. So, this which demands that more and more research will have to be conducted in making more and more benefits available to the common man of this particular country.

It is also important to understand that it is not only the researchers who have the complete responsibility to follow ethics. It is also important that the research participants follow certain or fulfill certain expectations. So, whatever has been described in research they have to follow appropriately. It is explained in the informed consent form and so there is a great need for including bioethics in the medical curriculum which is being stressed.

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There is certainly a hope because ethics in the practice of public health and in health research is being increasingly addressed. We know that there are challenges as well because the public expectations and demands are continuously increasing, but we will continue to find solutions and this has to be an ongoing process. For this, various public health stakeholders like public health system, policy makers, researchers and program managers, they should show adequate sensitivity and realize that we always can improve and a practice always can improve.

Thank you very much for your attention.