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# Ethical aspects in research with children

## Aspectos éticos en la investigación con niños

Nancy Piedad Molina Montoya*

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ABSTRACT

Research with children helps to produce knowledge for the improvement of their well-being. The vulnerability of minors, aspects concerning their participation in decision-making, as well as the asymmetry of their relationship with adults generate particular ethical issues and highlight the need for this population to receive special attention. *Objective:* To examine ethical aspects that should be considered when designing and developing research with the participation of children. *Materials and methods:* A search and documentary review was carried out in the EBSCO and SciELO databases, in addition to including texts and other documents on the subject. The categories and subcategories identified were used as thematic axes. Information was selected from the publication period of 1976-2017. *Conclusion:* The design and development of ethical research requires that researchers propose relevant questions; use sound theoretical assumptions and adequate methodologies; know the characteristics, needs and expectations of children; and comply with the core principles of research. These principles include respect for people, beneficence and justice—which is materialized in research contexts in the informed consent and assent—, guarantee of confidentiality and privacy, risk-benefit balance, equitable selection of research subjects, equitable distribution of benefits, balance of power relationships, and considerations about economic retribution to participants.

**Keywords:** ethics, bioethics, research, informed consent, children.

* OD, PhD in Bioethics. Associate professor at La Salle University, Bogotá, Colombia. nanmolina@unisalle.edu.co

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RESUMEN
La investigación con niños contribuye a producir conocimiento para la promoción de su bienestar. La vulnerabilidad de los menores, así como los aspectos concernientes a su participación en la toma de decisiones y la asimetría en su relación con los adultos, generan cuestiones éticas particulares y subrayan la necesidad de que esta población reciba atención especial. *Objetivo*: indagar sobre los aspectos éticos que deben considerarse para el diseño y el desarrollo de investigaciones en las que participen niños. *Materiales y métodos*: búsqueda y revisión documental en EBSCO y SciELO; además, se incluyeron textos y otros documentos sobre el tema. Las categorías y subcategorías identificadas se usaron como ejes temáticos. La información seleccionada pertenece al periodo de publicación 1976-2017. *Conclusión*: el diseño y desarrollo de investigaciones éticas implica que los investigadores planteen preguntas relevantes, utilicen presupuestos teóricos sólidos y metodologías adecuadas, conozcan las características, necesidades y expectativas de los niños y den cumplimiento a los principios nucleares de la investigación: respeto a las personas, beneficencia y justicia —que en el contexto investigativo se materializan en el consentimiento y asentimiento informados—, garantía de la confidencialidad y la privacidad, balance riesgo-beneficio, selección equitativa de los sujetos de investigación, distribución equitativa de los beneficios, balance de las relaciones de poder y consideraciones sobre la retribución económica a los participantes.

**Palabras clave:** ética, bioética, investigación, consentimiento informado, niños.

## INTRODUCTION

Research with children is necessary to obtain and produce knowledge that results in their health and well-being (1). These kinds of studies are justified because the pathophysiology of children is different from adults (2,3), and there are conditions that occur in childhood that can cause sequelae in the development process (4). Another argument for developing studies in pediatric patients is that pharmacological studies with adults can't be extrapolated to this population, mainly due to variations in pharmacokinetics (5) and pharmacodynamic responses (6), generating the risk of administering ineffective treatments, inadequate doses and producing unexpected adverse reactions (6-9). Children are not small adults and, therefore, in order for pharmacological therapy to be effective, its administration must meet their needs (10).

The topics of study in pediatrics include normal development, evolution and etiology of pathologies, promotion of health care, diagnosis, evaluation and treatment of childhood diseases (4). The development of research with minors implies the adoption of high scientific and ethical standards, in addition to considering several factors. Sigaud et al. (11) point out that it is a priority to take into account their individual needs and characteristics, as well as their patterns of thinking, feeling and acting at different stages of development.

In addition, certain aspects of children, such as the lack of capacity to consent, vulnerability and the asymmetry of their relationships with adults, generate particular ethical issues that cause the regulatory bodies to insist that they receive special attention (2,12-14). This implies that research in this population must meet certain requirements and emphasizes the roles of the researcher as manager of the studies and of the ethics committees as consultants, evaluators and supervisors of the process.

The research with children must be honest and transparent; they must be informed about it in a sincere, empathetic, authentic and coherent manner (15). This generates trust in them and their families (16). This attitude from the researchers demonstrates understanding, acceptance and interest, even in the face of their refusal to participate in data collection (17).

In addition, the studies must respond to research questions relevant to children, their families or the community, based on sound scientific concepts

that have no valid and extrapolated information from other studies, use appropriate methods for this population and that tend to produce valid conclusions and the subsequent publication of new information (1,11). The research methodologies must be sensitive to the particular interests or competencies of children to facilitate their participation (17). Likewise, research environments must be friendly and provide emotional, psychological and physical security for them and their families (1).

Researchers and ethics committees have a moral obligation to protect the dignity and well-being of the participants. The former is achieved by keeping up to date and ensuring the design and execution of scientifically and ethically appropriate projects that are relevant to society. The latter, on the other hand, is achieved by educating and advising the researchers and other actors involved in the research process, on their ethical, legal and scientific responsibilities, as well as doing the analysis, evaluation and monitoring of the development of the investigation to verify the compliance of such budgets.

## MATERIALS AND METHODS

This is a documentary review article that seeks to investigate the ethical aspects to be taken into account in the design and conduction of research involving children. The search for articles was done in the EBSCO database and in the electronic library sciELO, based on the MeSH (Medical Subjects Headings) terms *ethics*, *bioethics*, *research*, and *children* in English and Spanish. The period of publication of the articles was from 1976 to 2017. It took into account the articles that allowed the fulfillment of the stated objective. Additionally, a review of the subject was made in books and electronic documents.

The abstracts of the articles were read and those that corresponded with the objective were chosen. A complete reading of each article was made, identifying the main and secondary categories on the ethical aspects in the research with children, and they were taken as axes for the theoretical development, the segments of relevant material were selected and citations were grouped in the previously defined axes to generate the final document.

## RESULTS

The development of ethical research involves not only the collection of information, but also the dignity, rights and well-being of the participants (18,19); therefore, for a research project to be planned and executed with ethical criteria, it is necessary to understand and apply the core principles that guide it: respect for people, beneficence, and justice. Some rules that allow their compliance should also be taken into account.

### Respect for people

This principle implies assuming that all individuals are autonomous agents and that those with diminished autonomy have the right to be protected (20). Thus, respect for people implies their autonomy. The word *autonomy* comes from the Greek language and means "self-government." Thus, an individual is considered to be autonomous when he acts freely according to a plan chosen by him. Respect for a person's autonomy is achieved when he is recognized as having the right to maintain his point of view, to choose and to act based on his values and beliefs (21).

In the case of children, their autonomy is considered to be developing, and respect consists in making them be involved in decision-making about their participation in research. When they do not have enough maturity, their parents must represent them. Respect for autonomy, in the context of research, is materialized through informed consent and assent, as well as compliance with confidentiality and privacy rules.

***Consent and informed consent***

The use of these concepts points to an important difference between the agreement from adults and children to participate in research (22), and while *consent* describes the positive agreement of the person, *assent* refers to acquiescence (2).

Informed consent is an interactive process between the researcher and the subject that involves communication, discussion and feedback on the purposes, procedures, risks, benefits, and scope of the research, resulting in informed, free and voluntary participation. From this definition, it is noted that several elements are involved in the consent process: information, competence, voluntariness, validity, and authenticity (23).

An important element of consent is to provide clear, complete and detailed information necessary for decision-making. Researchers must ensure that they speak in a language that corresponds to the educational level of the person being informed, indicate the purpose of the research, what the participation will entail, the procedures to be carried out, the risks and benefits, the therapeutic alternatives, the adverse effects, how the results will be reported when the study involves diagnostic tests, and how support or counseling will be provided to the participants in case the results reflect the existence of any disease.

The researchers must make sure that the person being informed has understood the information and should be encouraged to give feedback about the information, in order to provide additional explanation, if required. Consent also implies competence, that is, the mental capacity to understand all aspects of research and the expression of a coherent decision (17,22,24,25). The parents of the minors give consent for their participation in the investigation and guide their decision when they do not have the capacity to make decisions (26).

Consent shall be valid if the information provided has been appropriate and enables decision-making and consent has been expressed voluntarily and free of coercion (23).

Although it has been stated that parents give consent for their children to participate in research, the regulations in some countries allow young people over the age of 14 years (27) and those over 16 years of age, in others, to give their consent (28) because they have a capacity to make decisions similar to adults.

It should be noted that autonomous decision-making is slowly evolving in minors, along with the cognitive and psychosocial aspects, and that respect for this autonomy in development and for their dignity deserves their inclusion in decision-making about their participation in research consistent with their capacity level (27,29).

The ability to make decisions reflected as understanding and competence is connected to the process of thinking. Because of their variation in development during childhood, objective determination of the child's ability to understand complex research-related issues is a major challenge for researchers (30). Studies suggest that children over the age of nine can understand most aspects of research (31).

Informed assent refers to the manifest agreement and free expression of the child to participate in the research (12,13,22). Although it is not appropriate to give an exact age at which the child can agree, there is a consensus that after seven years, children can give their assent (12,32,33). Seeking assent shows respect and gives the child the opportunity to say "no" to participating in research (13,26).

The conscious agreement of the child requires the researcher to provide information in clear and age-appropriate language and to use, if necessary, graphic or audiovisual resources that make it easy to understand the main aspects of the research (17,34). Likewise, a space of communication must be opened to resolve the doubts that minors may have about the research (1,35). Providing explana-

tions with language familiar to children increases the likelihood that they will receive and understand information about the study (22).

Table 1 summarizes the consent and/or assent requirements in research with children (12,27); however, it is necessary for researchers to take into account the regulations of the country where the research is to be carried out. In Colombia, in order to conduct investigations with minors, in any case, the Informed Consent should be obtained from those who exercise parental authority or legal representation of the child and when the child's capacity allows it, acceptance to be a subject of investigation —that is, their assent. This capacity must be certified by competent professionals (neurologist, psychiatrist or psychologist) (36).

TABLE 1. **Requirements of informed consent and/or assent in research according to children's age**

| Age | Characteristics | Requirement |
|---|---|---|
| Children without assent capacity | They do not have the ability to enter into any discussion about the research and it is up to the parents to watch over their well-being. | Consent from parents or attendants |
| School children | They understand most of the aspects related to their participation, but remain vulnerable to coercion or may be vulnerable in other respects. | Consent of parents or guardians; informed assent from the age of 7 |
| 14-year-old children or older | They understand and have similar capacity than adults. | Minor's consent; Parents' consent (not needed in some circumstances) |

Source: Own elaboration, based on Davidson y O'brien (12), Ackerman (27) y National Health and Medical Research Council, Australian Government (37).

There are two situations in which consent raises important ethical issues: on one hand, when the child or teenager gives his assent and parents do not give their consent. In Colombia, this minor would not be able to participate in research because normativity requires the consent of parents always. On the other hand, when the parents' consent has been obtained, but the child does not agree. In these circumstances, it is inappropriate to proceed with the research, unless it has been previously established that there is a benefit to the child or that the child is not mature enough to agree (12).

In order to make decisions, the complexity of the decision must be taken into account, in addition to the maturity of the child. More serious decisions involving consequences or important consequences for the future life will require high maturity and parental involvement in the process (25). Consequently, the degree to which the autonomy of decisions taken by the minor may be limited to protect his or her well-being should be weighed by the parents, taking into account the child's maturity criteria and the severity of the decision to be made.

### *Confidentiality and privacy*

These two rules allow compliance with the autonomy of the subjects (38). The right to confidentiality means that participants should not be recognized for their answers and the right to privacy means that participants must decide how much information they want to share with others. Privacy implies, on the one hand, anonymity, and on the other, secrecy—that is, information should not be disclosed to third parties without the explicit consent of research subjects (22,39).

Confidentiality and anonymity must be explained in a way that children can understand how the information obtained will be handled and used. Chapter 1, Article 8 of Resolution 8430 of 1993 states that, in research on human beings, the privacy of the individual or subject of research will be protected. In terms of information management, researchers should consider several key points (17):

- Collect and preserve the minimum amount of data required.
- Personal data must be used only for the purpose specified in the consent, unless otherwise agreed by the participant, and cannot be retained after the initial purpose has ceased.
- Encoding strategies should always be created to avoid the use of personal data in the processing of information.

- Access to data by third parties depends on the prior consent obtained from the research participants.

- Confidentiality and privacy guarantees must always be respected.

- It should be clear how long the information will be kept, how it will be stored and who will have access to it.

## Beneficence

This principle involves the obligation related to two specific actions: 1. Do not cause harm; and 2. Maximize benefits and reduce damages (40). The application of this principle leads to reflection and consideration on the level of risk to which children may be exposed. This refers to possible damages (physical, psychological, social) that may arise from the investigation (1,39).

It is necessary to have clear parameters for the classification of researches according to type of risk. Guidelines to assist ethics committees in evaluating research with children, formulated in 1980, posed the following classification: negligible risk, minimal risk, and greater than minimum risk. The former implies a lower risk than that which occurs in situations of everyday life, the second is a greater risk than the first, and the third is one in which the probabilities of affecting the subject are significant (40). In Colombia, risk classification is regulated in Title 1, Article 9 of Resolution 8430 of 1993 (36) (Table 2).

### *Risk-benefit balance*

When considering whether the research proposal is justified, the risks to the child must be balanced with the probable benefits for him, his family and the community (1). If possible, information on previous animal studies or healthy groups should be provided as basis for risk assessment by including individuals (41).

Researcher must take all reasonable precautions to ensure that children will not be adversely affected by participation in the study (42). Keep in mind that potential risks may persist in them for a longer time, since they are younger than the average participants of the investigation (43). The acceptable level of risk will depend on the importance of the study and the tendency to directly benefit the participants. In this type of research, the level of risk should be lower compared to adult participants (1). While in some studies it is easier to identify the risk of harm, in others it is not so simple. Some studies considered to be at low risk may cause different types of damage, such as anguish or stigma and, in contrast, others considered to be at high risk may minimize their impact on the population by adopting adequate protective measures (39).

table 2. **Classification of research according to risk in Colombia**

| Risk level | Type of study | Techniques |
|---|---|---|
| No risk research | Documentary research, retrospective studies, research without intervention or without intentional modification of biological, physiological, psychological or social variables of the individuals participating in the study | Review of medical records, interviews, questionnaires and others in which no sensitive aspects of their behavior are identified or treated |
| Minimal risk research | Prospective studies with data from common procedures | Diagnostic physical or psychological examinations or routine treatments |
| More than minimal risk research | Studies in which the probabilities of affecting the subject are significant: radiological and microwave studies, drug studies, radioactive isotope investigations, and generators of ionizing or electromagnetic radiation, among others | Tests with new devices, studies that include surgical procedures, blood extraction greater than 2% of circulating volume in neonates, amniocentesis and other invasive techniques or larger procedures, those using random methods of allocation to therapeutic schemes and those with control with placebos, among others |

Source: Own elaboration, based on Resolution 8430 of 1993 (36).

This implies the need to reflect in depth on the scope of the investigation, in order to clearly identify the possible risks of the participants to not over or underestimate them, so as to take adequate measures for the protection of the kids. In addition, the benefits for participants and society must be clearly identified in order to be able to analyze the risk-benefit balance.

International guidelines for research with minors advocate for a standard of "minimal risk," which implies that the anticipated probability and magnitude of the harm do not have to be greater than those ordinarily found during physical or psychological activities in daily life (39). However, researchers, ethics committees and community are responsible for assessing whether scientific value and benefit to society warrant studies that involve a greater risk than the minimum for children, an aspect in which they must take into account the regulations of the country where the investigation is carried out.

In Colombia, the regulation states the developing of "minimal risk" research and "more than minimal" with minors in specific circumstances as determined in Title I, Chapter III of Resolution 8430 of 1993 (36). When studies can lead to a pre-symptomatic diagnosis of a disease, the family should receive an explanation on how support and counseling will be provided if the diagnostic test is positive (1).

## Justice

In the case of research with children, this principle implies the right to fair treatment, which harmonizes as far as possible the asymmetry in power relations, equitable selection and equality of opportunity in the distribution of risks and benefits of the study (12,27).

It is against the principle of justice, the exclusion of children and adolescents in research projects when the study answers pertinent questions that can produce valuable knowledge for their well-being.

## Selection of research subjects

Unequal selection of research subjects could occur if subjects of certain subgroups of the socioeconomically disadvantaged population are selected, who have already made public service sacrifices or who have been repeatedly recruited in the research. Researchers should make sure to avoid such behaviors, as well as take advantage of the vulnerability of participants and create mechanisms to match protection for all (44).

The inclusion of the participants depends on the objectives and scope of the research. It is suggested that researchers offer all eligible individuals the same opportunities to participate and avoid discriminatory behavior (45). On the other hand, the groups that will be selected to investigate should be related to the research question and not to the researchers' convenience (46).

The inclusion of children in research contributes to our commitment to research justice by improving our knowledge and ability to respond to their unique needs throughout their development. An example of equitable selection is eligibility to participate in clinical trials, as the resulting benefits should be available to all children with serious illness for whom current treatment is unsatisfactory (27).

### *Power relationships*

In several contexts, adults tend to be perceived as more powerful than children. This is also observed in the research environment. There are several ways to explore power relationships between subjects and researchers in order to balance them. It has been considered that participatory methods and reflexivity can help in this task (47).

Other researchers say that it is not necessary to use methodologies, rather than those consistent with children's experiences, interests, values and daily routines that attend to the their actions, meanings and use of language to establish a dialogue

in which the researcher has a better understanding of the interactions and social relations of the children (48).

***Equitable distribution of risks and benefits***

The ethical distribution of the burdens and benefits of research implies that the participants are not denied the benefit to which they are entitled and that none of them are in particular risks or undue difficulties (49).

All research subjects should be treated fairly, assigning research burdens based on ethical criteria. The core principles of research require children to take the risks that are strictly necessary during research. For example, they should not be asked to bear the risks of research solely to benefit adults (44).

Once the investigation is completed, justice requires an equitable distribution of the benefits derived from successful investigations. This distribution should ensure the benefit not only of participants but of all children, taking care that they are not excluded by factors such as poverty or marginalization (44).

***Economic retribution in research***

Although offering some kind of incentive or compensation to the families improves the recruitment, this raises ethical questions because the one who takes the risk is the child and not his family. Additionally, it is possible that the payment does not justify the risk to which the child is exposed and that the guardians may undervalue the risks or ignore them to receive the compensation (13). Four types of retribution have been identified in the field of research: reimbursement, compensation, recognition, and incentive (13).

Reimbursement seeks to return to participants the money invested in the expenses they have incurred to participate in research such as transportation, food, accommodation and child care. This form of retribution conforms to the principle of justice, and ensures that the participants of the investigation are treated fairly (49).

In some contexts, the economic or social situation of children or families may be affected by their participation in research. Compensation refers to rewarding children or their families for their time, work and effort, and for any inconvenience caused by their participation (for example, loss of income). The ethical principle of justice requires recognition of the contribution of children and the principle of non-maleficence underpins the obligation of researchers to ensure that potential harms of research, such as loss of income, are evaluated, minimized or removed (49).

Recognition takes the form of gratifications given to children after their participation in order to acknowledge and thank their contribution to the research. This form of remuneration reflects reciprocity in the provision of direct benefits to the participant as a result of his participation in the research. Ideally, if this form of remuneration is contemplated, the participants in the investigation should know whether they have given their consent to participate in the investigation or when data collection has been completed (49).

The incentive is designed to encourage the participation of children in research. These may be alternative payments such as vouchers for a known store or cellphone credit. Incentives can be considered as a means of persuasion by indicating to potential participants that participation in research generates an economic benefit.

Ethical rules of participation in research require that acceptance to participate is freely given—that is, that the person cannot be coerced or unduly influenced by psychological, financial or other pressures. Researchers should take this into account and act with caution in this regard.

There are two possible approaches to solve this issue: One is the elimination of retributions for

research, and another is the adoption of measures to minimize the distortion of payment in decision making by parents (38).

In Colombia, Resolution 8430 (36) does not consider payment, remuneration or incentive in the investigation. It only contemplates the compensation in case the subject suffers damages as a result of the participation in this one.

As we have seen, research with children is framed within ethical principles that guide it and define the criteria that must be taken into account for its planning and execution. However, it is the researchers and ethics committees who must ensure that they are applied and verified, and that they fulfill various roles and responsibilities in the research, as we shall see below.

### Role of the researcher

The role of the researcher is to ensure the safety, rights and well-being of study participants. Their responsibilities in the development of research with children and adolescents include (34,50):

- Being suitable and updated about the clinical and research procedures, as well as about the design and execution of research.
- Ensuring that research protocols involving children are under scientific and ethical standards.
- Conducting research as described in the approved protocol.
- Identifying potential conflicts of interest for affected parties.
- Ensuring that research participants give their consent and/or assent and verifying their relevance and validity during the research process.
- Communicating with the children and adolescents participating in the research in a manner appropriate to their development—and also guide their parents—about what to expect during the progress of the research.
- Conducting appropriate safety oversight by monitoring and reporting adverse events.
- Reporting violations, errors or problems to the corresponding entity: sponsors, regulators or ethics committees.
- Communicating research results to the community, the public and participants.

### Role of the research ethics committees

These are interdisciplinary collegial bodies of deliberative and consultative character in charge of analyzing and advising to the investigators and the community on the ethical questions that arise in the research scope. Therefore, their work in the research process includes (34,50):

- Educating its members on the ethical, legal and scientific norms to approve the investigations that involve children and adolescents and to realize their proper interpretation.
- Educating researchers conducting studies that involve children and adolescents about their specific ethical, legal, and scientific responsibilities.
- Applying ethical and regulatory standards to the review and initial or continued approval of research protocols, including careful evaluation and categorization of risks.
- Verifying that studies have been scientifically evaluated by peers with proven health and research experience with children.
- Verifying the suitability of researchers to conduct research with children and adolescents.

- Making available materials and resources in research with children, including information on ethics on such research at educational sites and programs.

- Conducting assessments to guide improvements in the committee's performance in assessing and monitoring research involving children.

- Developing specific policies and guidelines for important topics, with additional guidance to committee members and researchers.

## CONCLUSIONS

The design and execution of research with children implies that researchers:

- Protect their integrity and ensure their well-being.

- Ask relevant research questions.

- Use sound theoretical assumptions and appropriate methodologies.

- Know the characteristics, needs and expectations of the participants.

- Develop friendly, transparent and honest projects with children in environments where they feel safe.

- Comply with current regulations in their countries.

- Adopt and apply the core principles of research: respect for people, beneficence and justice, which in the context of research are materialized in obtaining informed consent and assent, guarantee of confidentiality and privacy, benefit risk balance, the equitable selection of research subjects, equitable distribution of benefits, the balance of power relations, and considerations of economic retribution to participants.

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