

## Ethical Issues Related to Children


### ChildrenGenoNetwork

**D. F. Merlo**  
*National Cancer Research Institute, Genoa, Italy*



**L.E. Knudsen**  
*University of Copenhagen, Denmark*

**K.H. Vähäkangas**  
*Kuopio University, Finland*

D.F. Merlo  
Child Health & Environment  
Brussels, November 23-25, 2005



**The recognition of crimes, abuses, injustice, and discrimination perpetrated in the name of medical research (or science) has led to the identification of basic ethical research principles some 50 years ago<sup>1</sup>.**

<sup>1</sup> **The Nuremberg Code**

*"Measuring children's skulls and other attributes were part of the Nazi plan to catalogue every citizen's fitness."*

D.F. Merlo  
Child Health & Environment  
Brussels, November 23-25, 2005

## PUBLIC HEALTH POLICY ADVISORY BOARD

### Health and the American Child-Mortality Update 2001

Table 3: Leading Causes of Death, Children Ages 1-19, by Rank

Causes of Death	ICD Codes	1995		1998		1995		1998	
		Rank	Rank	Total	Total	% of Total	% of Total		
Unintentional Injury	800-949	1	1	12,447	11,779	41.4	44.0		
Homicide	960-969	2	2	4,275	3,139	14.2	11.7		
Suicide	950-959	3	4	2,227	2,061	7.4	7.7		
Cancer	140-208	4	3	2,205	2,098	7.3	7.8		
Congenital anomalies	740-759	5	5	1,395	1,151	4.6	4.3		
Heart Conditions	390-398/402/404-429	6	6	944	955	3.1	3.6		
HIV	042-044	7	10	455	110	1.5	0.4		
Pneumonia/Influenza	480-487	8	7	367	342	1.2	1.3		
*COPD	490-496	9	8	312	299	1.0	1.1		
*Cereb. / Vas. Diseases	038	10	9	176	183	0.6	0.7		
Others				5,270	4,713	17.5	17.6		
<b>TOTAL</b>				<b>30,078</b>	<b>26,830</b>	<b>~100.0</b>	<b>~100.0</b>		

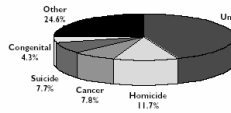
\*COPD-Chronic Obstructive Pulmonary Diseases and allied conditions  
\*Cereb./Vas. - Cerebrovascular Diseases  
ICD codes - International Classification of Disease Codes  
Source: CDC Wonder Mortality Statistics: Centers for Disease Control and Prevention; 2001

D.F. Merlo  
Child Health & Environment  
Brussels, November 23-25, 2005

## PUBLIC HEALTH POLICY ADVISORY BOARD

### Health and the American Child-Mortality Update 2001

Figure 2: Percent Distribution of Mortality in Children (Ages 1-19) by Cause, 1998



Source: CDC Wonder Mortality Statistics: Centers for Disease Control and Prevention; 2001

D.F. Merlo  
Child Health & Environment  
Brussels, November 23-25, 2005

**... principles.... concern medical experiments on human beings aimed at gathering results that are for the good of society and unprocurable by other methods or means of study.....**

**...and ....**

**individuals participating in research have the right to know about the consequences of research to their life and health**

D.F. Merlo  
Child Health & Environment  
Brussels, November 23-25, 2005

**... scientists carrying out the research must conform to the ethics of the medical profession to satisfy moral, ethical and legal concepts**

**A. therapeutic research (e.g., randomised clinical trials) with the aim of investigating treatment(s) that might benefit the sick**

**B. non-therapeutic research (e.g., environmental health studies) aiming at acquiring knowledge that usually is of no immediate benefit to the study participants**

D.F. Merlo  
Child Health & Environment  
Brussels, November 23-25, 2005

# CHILD HEALTH AND THE ENVIRONMENT: RESULTS FROM EU FRAMEWORK 5

**... scientists carrying out the research must conform to the ethics of the medical profession to satisfy moral, ethical and legal concepts**

**A. therapeutic research** } **risk? benefit? knowledge**  
**B. non-therapeutic** } **risk? benefit? knowledge**

**Communicate**  
**Inform**  
**Consent**

**participate**

D.F. Merlo Child Health & Environment  
Brussels, November 23-25, 2005 7

**.... Being certain that your pediatric trial subjects and their parents are making informed decisions requires a unique consent process.**

*Siman & Johnson, Appl Clin Trials (11) 7, 46-56, 2002*

D.F. Merlo

**“The voluntary consent of the human subjects is absolutely essential” for research involving human experimentation (research) to be ethical.**

**EU fundamental rights: Article 3: integrity of a person “within medicine and biology ....respect free and informed consent .....according to the law....”**

D.F. Merlo Child Health & Environment  
Brussels, November 23-25, 2005 9

**.....implementation of the basic ethical principles results in detailed ethical guidelines for therapeutic and non-therapeutic research**

**.....guidelines promote the following four basic principles of biomedical ethics:**

**Autonomy: respect for the person**  
**Beneficence: maximizing possible benefits**  
**Non-maleficence: minimizing possible risks**  
**Justice: fairness of research**

D.F. Merlo Child Health & Environment  
Brussels, November 23-25, 2005 10

Organisation	Website	Content
ASHG	<a href="http://www.faseb.org/genetics">www.faseb.org/genetics</a>	DNA banking and analysis
CIOMS	<a href="http://www.cioms.ch/frame_guidelines_nov_2002.htm">http://www.cioms.ch/frame_guidelines_nov_2002.htm</a>	International ethical guidelines for biomedical research involving human subjects
HGP	<a href="http://www.ornl.gov/TechResources/Human_Genome/">www.ornl.gov/TechResources/Human_Genome/</a>	NCHGR-DOE Guidance on Human Subjects issues in Large-Scale DNA sequencing
EMEA	<a href="http://www.emea.eu.int">www.emea.eu.int</a>	CHMP position paper on the terminology of pharmacogenetics (3070/01)
IPA	<a href="http://www.ipa-world.org">www.ipa-world.org</a>	One of the key areas: Children's environmental health
NBAC, USA	<a href="http://www.bioethics.gov">www.bioethics.gov</a>	Ethical and policy issues in research involving human participants
Nuffield Council on Bioethics	<a href="http://www.nuffieldbioethics.org">www.nuffieldbioethics.org</a>	Ethical issues on research e.g. in health care in developing countries, using human tissues, and genetics and human behaviour
Unesco	<a href="http://www.unesdoc.unesco.org">www.unesdoc.unesco.org</a>	The Universal Declaration on the Human Genome and Human Rights – from theory to practise
WMA	<a href="http://www.wma.net">www.wma.net</a>	Declaration of Helsinki
ASA	<a href="http://www.amstat.org">http://www.amstat.org</a>	Privacy, Confidentiality, and Data Security

D.F. Merlo Child Health & Environment  
Brussels, November 23-25, 2005 11

**Autonomy**

- **right to know and not to know and freedom in making decisions : to or not to participate in or withdraw from the research**
- **requires written informed consent which can only be based on adequate and relevant information to potential research participants**
- **only understood information can guarantee a free-will decision**
- **autonomy is specifically relevant to children, who, due to age-related reasons (physical, mental, and psychological development) are a vulnerable subset of the human population and deserve protection**

D.F. Merlo Child Health & Environment  
Brussels, November 23-25, 2005 12

**Research with and on children is necessary** both within the clinical and environmental fields to provide age-specific relevant data regarding:

- efficacy and safety of medical treatments
- risk assessment from unintended environmental exposures

---

• Then.....

- **Research - findings - actions (priorities?)**
- **Disease burden = priority (?)**
- [orphan drugs, -exposures, - adverse outcomes]
- Weak risks [community] vs strong risks [subjects]

D.F. Merlo Child Health & Environment Brussels, November 23-25, 2005 13

**Consensus: children should give their own opinion, in the form of written consent, whenever possible, on the studies they attend**

Figure 2: Percent Distribution of Mortality in Children (Ages 1-19) by Cause, 1998

Source: CDC Wonder Mortality Statistics: Centers for Disease Control and Prevention; 2001

**best interest .**

**Consensus agreement that a "consent dyad" is required to conduct research on children**

D.F. Merlo Child Health & Environment Brussels, November 23-25, 2005 14

**Obtaining informed consent from children, involves necessarily child's assent and parental (or legal guardian's) consent (proxy consent).**

(proxy consent: dismissed - a true consent cannot be given by another person).

**Obtaining informed consent from children, involves necessarily child's assent and parental (or legal guardian's) permission**

D.F. Merlo Child Health & Environment Brussels, November 23-25, 2005 15

Dominion	Developmental stages				
	Prenatal		Infancy /Childhood		Adulthood*
	Fetus	Newborns	Infants	Childhood	Adolescence
Demography	0	0	<2 years old	(>2, <=14)	>14 years old
Biological relationship and possible forms of permission to research	Parents* <sup>**</sup> : Informed permission		Parents** Informed permission		Parents***: Informed permission
	Fetus: Implicit assent		Infant: Implicit assent	Child: Assent	Child: Assent / Consent (>14)
Philosophy	Human being status recognized only when full capability of free decision is reached			Full capability of free decision (age, maturity)	
Religion	Status as a human being recognized from conception on				
Ethics	Ethical regulators: decisions apply to all ages				
Law	Status as a human and requirement/possibility for individual consent depending on national legislations				

D.F. Merlo Child Health & Environment Brussels, November 23-25, 2005 16

**The protocols for all randomised controlled trials (RCTs) or other studies carried out on human subjects in Europe must now, in practice be submitted to appropriate local or regional Research Ethics Committees (RECs) for ethical approval.**

**Depending on whether national legislation exists on the research on humans, RECs may have either national, regional (major city or group of counties) or local (e.g., local area, institutional, hospital) responsibilities, or responsibilities for group of States.**

D.F. Merlo Child Health & Environment Brussels, November 23-25, 2005 17

**The European countries are divided by those using regional committees and those using local committees.**

**At least in the UK and in Finland both regional and local committees have a role. However, in Finland only the regional central hospital district committees have a legal, official role.**

**In those cases where ethics committees are locally/institutionally based like in Poland, Italy, RECs are much more numerous**


D.F. Merlo Child Health & Environment Brussels, November 23-25, 2005 18



**•The composition of committees varies considerably across Europe**  
**Size: between five and sixteen members**  
**Multidisciplinarity frequent:**  
medical doctors, general practitioners, lawyers, ethicists, psychologists, nurses, pharmacists, statisticians and theologians

**•This degree of variation in composition (both numerical and expertise terms) shows a limited uniformity across Europe**

D.F. Merlo Child Health & Environment  
Brussels, November 23-25, 2005 19



**RECs assess the scientific validity, the value of the proposed research, and the privacy issue.**

**Since the design of the study is the key aspect of any research, RECs should be properly equipped to judge this part of the written protocol.**

*epidemiologists, biostatisticians, and pharmacologists, toxicologists, etc.. These professions can provide expertise in judging the quality of design and foreseen risk for the children involved in the research.*

D.F. Merlo Child Health & Environment  
Brussels, November 23-25, 2005 20




**A need for harmonisation in appointment, composition and procedures for assessing applications has been described in several reports to the EU commission [a].**

**For studies including children the involvement of a paediatrician should always take place.**

[a] *Beyleveld D., Townend D. and Wright J. (eds), Research Ethics Committees, Data Protection and Medical Research in European Countries, Ashgate Publishing Limited, (2005).*


D.F. Merlo Child Health & Environment  
Brussels, November 23-25, 2005 21



**Consensus**

- children should be always respected as persons;
- children assent/consent and parental permission should be sought whenever possible by using appropriate tools;
- the abstract description of the research for getting research participants' informed permission /assent / consent must be written in understandable language according to the age of the target group(s);
- in studies involving children at least two information sheets are required: one for children and one for their parents;

D.F. Merlo Child Health & Environment  
Brussels, November 23-25, 2005 22



- enough time should be given for parents and children to discuss the research and consider their participation in a friendly environment;
- refusal to participate by a child should be respected;
- follow-up tools must be considered by researchers to monitor long term effects in study participants, considering incidental findings;
- children from different countries or belonging to different ethnic, social or religious groups should be treated with the same respect

D.F. Merlo Child Health & Environment  
Brussels, November 23-25, 2005 23