Commission of the Bishops' Conferences
of the European Community

COMECE

Ethical assessment of clinical trials on medicinal products

Respect and protection of vulnerable persons and populations

(Translated from French)

Commission of the Bishops' Conferences of the European Community

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RESPECT AND PROTECTION OF VULNERABLE PERSONS AND POPULATIONS

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OF CLINICAL TRIALS ON MEDICINAL PRODUCTS
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EXECUTIVE SUMMARY

Last year, the European Commission published its Proposal for a Regulation on clinical trials on medicinal products for human use aiming to relaunch clinical research in the European Union while ensuring the optimal protection level for participants and the reliability of the data obtained.

The COMECE Secretariat welcomed this proposal and closely monitored this project from the start of the Commission's public consultation process.

As the voting date by the competent parliamentary committee approaches, the COMECE Bioethics Reflection Group is publishing the current opinion which stresses the following key points:

1. The simplification and harmonisation of the assessment and authorisation procedures of clinical trials on medicinal products between Member States is completely acceptable insofar as its fulfilment does not create an obstacle to an independent, rigorous application of every research project and fully respects the rules on the division of competences between European Union and Member States.

2. Within the framework of the Proposal for a Regulation, it would be ethically wrong to deem parts I and II of the assessment report as two completely separate reports.

3. Moreover, it is essential to ensure that rules on the assessment of protocols should be compatible with the diversity of bodies – regrouping persons with a wide range of competences – in charge of this assessment in the countries of the Union, and with the requirements formulated on their functioning. This verification must focus on the deadlines given to the bodies in charge of the evaluation to render their decision.

4. The recognition of human dignity also leads to recognition and appreciation of the value of voluntary participation in research projects for the good of the community and to a prohibition of "*making the human body and its parts as a source of financial gain*" by granting financial incentives to any person agreeing to take part in some medical research.

5. A key ethical point of research carried out on human subjects is that of respecting and protecting particularly vulnerable people and populations who could be unduly used as easily exploitable objects for experiments.

6. It is undeniably crucial that various groups of patients may be subject to research

on medicinal products and that they should not be deprived of duly validated medicinal products adapted to their condition. However, "*medical research involving a disadvantaged or vulnerable population or community is only justified if the research is responsive to the health needs and priorities of this population or community and if there is a reasonable likelihood that this population or community stands to benefit from the results of the research.*"

7. The subject of the research may agree to become involved in a research protocol that does not fully respond to the individual's own interest but will do so for the good of others, in the "*medical interest of the community*" and consequently for the "*common good*", insofar as the patient's physical or psychological integrity is not endangered.

8. Hence we derive the general principle that trial subjects must not be sacrificed in the interests of science or of the community of patients, and that every person involved in a research project must have consented to it.

9. Trial medicinal products may not be given to persons who are not capable of giving their consent except in cases where the same results cannot be obtained by resorting to persons capable of giving their consent and if the foreseeable benefits/predictable risks ratio is to their advantage.

10. As for clinical trials in emergency situations, the only acceptable research is specific research on individuals placed in such a situation that one may have good grounds for anticipating a direct benefit with regard to their condition and that would present a minimal risk and only impose a minimal burden. It is also important to give a sufficiently precise definition of the terms "*minimal risk*" and "*minimal burden*".

11. The obligation to respect populations from countries with limited resources should not obscure the duty of solidarity that consists, for developed countries and their institutions, in participating in the fight against endemic illnesses affecting millions of people in developing countries.

12. "*Equally important is to respect the strong desire, in developing countries, for assistance that helps them build their own R&D capacity to manage their own priority diseases and health needs.*"

In view of the important ethical values at stake, the COMECE Secretariat will continue to monitor this issue.

1. INTRODUCTION

On 4 April 2001, the European Parliament and Council adopted a Directive relating to "*good clinical practice in the conduct of clinical trials on medicinal products for human use*"[1].

Twelve years on, the EP and the Council are preparing to replace it by a Regulation that would be uniformly applied in all Member States. One of the key objectives of this substitution consists in simplifying and unifying the assessment and authorisation procedures of clinical trials for medicinal products between Member States. This objective is wholly acceptable if its realisation places no obstacle to a rigorous, independent assessment of any research project involving an intervention on human subjects and fully respects the rules of division of competences between the European Union and the Member States.

As stated in the Public Consultation on the Concept Paper submitted by the European Commission, "*ethical issues clearly fall within the ambit of Member States and should remain there*"[2]. It is thus crucial to clearly recognise the right of Member States to formulate ethical objections and to oppose the implementation of any research that would lead to such objections on their own territories.

1 *Directive 2001/20/EC of the European Parliament and of the Council of 4 April 2001 on the approximation of the laws, regulations and administrative provisions of the Member States relating to the implementation of good clinical practice in the conduct of clinical trials on medicinal products for human use.* Henceforth, this text will be cited as Directive 2001/20/CE.
http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2001:121:0034:0044:en.PDF

2 Cited in: *Contribution of the Secretariat of COMECE to the Public Consultation on the Concept Paper submitted by the European Commission: Revision of the 'Clinical Trials Directive' 2001/20/EC*, 12 May 2011.
http://ec.europa.eu/health/human-use/clinical-trials/developments/ct_public_consultation_2011_en.htm

2. ETHICAL ASSESSMENT OF RESEARCH PROJECTS AND REQUIRED CONDITIONS

The Proposal for a Regulation explicitly recognises that, in the assessment of research protocols "*a clear distinction between aspects where Member States cooperate in the assessment and aspects of an intrinsic ethical or national/local nature where the assessment is made by each Member State individually*"[3]. The fact remains that any rules ultimately adopted must make such an assessment possible.

The proposed Regulation stipulates: "*this distinction is without any prejudice as to the body which, in a Member State, performs the assessment […]. It does hence not regulate or harmonize the precise functioning of Ethics Committees.*"[4] However, it rightly requires that "*any application of a clinical trial will have to be assessed jointly by a reasonable number of persons who are independent, who have collectively the necessary qualifications and experience in all relevant fields, including the view of lay persons*"[5]. It is thus essential to verify that the rules concerning the assessment of the protocols are compatible with the diversity of the bodies in charge of this assessment in Member States, and with the requirements applicable to their functioning.

This verification should particularly focus on the deadlines granted to the bodies in charge of the assessments to deliver their decisions. For example, it is foreseen that each Member State has ten days before giving its opinion on Part II of the assessment report[6]. This Part focuses particularly on the ethical aspects of questions raised by the research project under examination. Yet, this assessment very often requires an in-depth study of the entire research protocol[7]. It would thus prove dubious to deem Parts I and II of the assessment report as two completely separate reports. Such a rigid understanding of the assessment procedure would be unacceptable. It

3 *Proposal for a Regulation of the European Parliament and of the Council on clinical trials on medicinal products for human use, and repealing Directive 2001/20/EC* (henceforth known as Proposal for a Regulation), Legal aspects of the Proposal § 3.2.
http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=COM:2012:0369:FIN:EN:PDF

4 Ibidem.

5 *Proposal for a Regulation*, Legal Aspects of the Proposal, § 3.2 and art. 9.

6 *Proposal for a Regulation*, art. 7.

7 We can read in § 3.2 of the Legal Aspects of the Proposal for a Regulation: "*The proposed Regulation does hence not regulate or harmonise the precise functioning of Ethics Committees (…) or limit the Ethics Committee's scope of the assessment to genuinely-ethical issue*". It is essential to note the reason given to this statement: "*science and ethics cannot be separated*".

is imperative that the ethical assessment of a research project take into account the whole situation in which the trial would put the persons "*participating*"[8] in such research.

This requires bringing together people who have all kinds of expertise[9]. In many cases, it is perhaps impossible to respect such a short deadline: a mere ten days! The sponsors obviously want to obtain their authorisations as quickly as possible, but granting such a short deadline for some assessments only shows up the lack of importance accorded to them.

However, according to the very same text of the Proposal for a Regulation, its objective is "*to ensure that, throughout the Union, clinical trial data are reliable and robust while ensuring the safety and rights of subjects*"[10]. "*This Regulation respects the fundamental rights and observes the principles recognized in particular by the Charter of Fundamental Rights of the European Union and notably human dignity, the integrity of the person, the rights of the child, respect for private and family life, the protection of personal data and the freedom of art and science*"[11]. There is already plenty of material for analysis and assessment!

8 We refer to the term used in the Proposal for a Regulation to define '*Subject*': "*an individual who participates in a clinical trial, either as recipient of an investigational medicinal product or as a control*" (Article 2: Definitions)

9 Cf. *Proposal for a Regulation*, art. 10.

10 *Proposal for a Regulation*, Consideration 66.

11 *Proposal for a Regulation*, Consideration 65.

3. RESPECT FOR HUMAN DIGNITY AND NOTION OF «*COMPENSATION FOR RESEARCH*»

Recognition of human dignity includes the respect of physical and mental integrity, consequently leading to the need to obtain, prior to any act of care or research and according to the very terms of the Charter of Fundamental Rights of the European Union, "*the free and informed consent of the person concerned, according to the procedures laid down by law*"[12], or failing that, the authorisation of the person's legal representative. The Proposal for a Regulation[13] clearly recognises this obligation.

But an ethical assessment cannot end there. Recognition of human dignity also leads to prohibition of "*making the human body and its parts as a source of financial gain*"[14].

Giving financial inducements to persons accepting to undergo a clinical trial raises a key ethical issue. The reimbursement of expenses incurred, the loss of income resulting from one's participation in a trial or the indemnification for any damage suffered[15] do not fall into the notion of "*gain*". On the other hand, it is really surprising to see the notion of "*compensation for participation in the clinical trial*" raise its head in the proposed Regulation even when the subjects involved in the trial are incapacitated adults or minors, whereas it is specified in the very same Regulation that "*no incentives or financial inducements are given*"[16]. Thus, it is essential to define and distinguish a fair "*compensation*" in the form of a reimbursement or indemnification from a true financial gain that would prove a more or less significant source of income stemming from the fact of having "*made one's body available to research*". This delicate ethical question calls for vigilance on the part of every Member State. This vigilance becomes even more important when the persons targeted for participation in clinical trials are more vulnerable and likely to be exploited.

Instead of using financial incentives to gather individual participation, every society

12 Cf. *Charter of Fundamental Rights of the European Union*, art. 3.

13 *Proposal for a Regulation*, art. 28, 1, c) and d).

14 *Charter of Fundamental Rights of the European Union*, art. 3.
http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:C:2010:083:0389:0403:EN:PDF

15 *Proposal for a Regulation*, art. 30 and 31.

16 *Proposal for a Regulation*, art. 30 and 31. OR Idem.

should recognise and appreciate the value of solidarity with and between patients – as indeed the aim of any clinical research consists in reaching general conclusions applicable for an entire group of patients –, thus recognizing and appreciating the value of voluntary participation in research projects for the common good of the community.

4. RESPECT AND PROTECTION OF PARTICULARLY VULNERABLE PERSONS AND POPULATIONS

These remarks prompt the COMECE Reflexion Group on Bioethics to focus once again[17] on a key point of the ethic of research on human subjects, that of respecting particularly vulnerable persons and populations, and the protection to which they have a right.

Particularly vulnerable persons and populations may, indeed, be unduly used by unscrupulous researchers or companies as easily exploitable objects of experimentation. Including persons or populations such as these in research proposals must be governed by extremely strict reservations and specific rules granting them all due protection. Here, complete transparency in the processes will provide an additional guarantee.

Without doubt, it is essential that the different categories of patients be subject to clinical trials and also that they should not be deprived of drug treatments adapted to their condition and duly validated. Young children, for example, suffer from the consequences of a lack of paediatrics validation for a wide range of drugs that are only tested on adults[18]. Furthermore, there is currently no treatment for a plethora of so-called "*orphan*" diseases. Some illnesses are not being researched at all due to the paucity of resources of the countries where they are widespread. "*There is an increasingly urgent need to fill the very serious and unacceptable gap that separates the developing world from the developed in terms of the capacity to develop biomedical research for the benefit of health-care assistance and to assist peoples*

17 In 2001, the Reflexion Group on Bioethics of the COMECE published an opinion on "*medical experiments*" and, in 2002, another opinion on "*biomedical research in developing countries*". Both are available in the *Science and Ethics* brochure, Brussels, June 2008, p. 52-53 and 46-47.
http://www.comece.eu/content/site/en/publications/pubsec/index2.html

18 Cf. World Health Organization (WHO), *Key policies on paediatric drugs*
http://www.who.int/childmedicines/media/backgrounder/fr/index.html
"*We do not know the effects of some drugs on children. This is partly due to the fact that less clinical trials are carried out on children than on adults. . […]. The lack of clinical trials on paediatric drugs leads to gaps in the information relating to the quality and safety of medications. These gaps discourage research pharmaceutical laboratories from research and developing drugs adapted to children, which also reflects on pharmaceutical companies manufacturing generic drugs at a lower cost*".

afflicted by chronic poverty and dire epidemics"[19].

The above-stated problem has been tackled by countless international recommendations, directives and conventions. We must recognise and salute their great value, taken as a whole. The regularly amended and updated Helsinki Declaration[20] remains the first reference in this area. Indeed, it is one of the foremost references of the European Directive of 4 April 2001. Articles 16 and 17 of the Convention on Human Rights and Biomedicine[21], its additional Protocol[22] on biomedical research and explanatory report[23] as well as the International Ethical Guidelines for Biomedical Research Involving Human Subjects[24] have also proved their worth. The Pontifical Council for Health Pastoral Care also contributed through its Charter for Health Care Workers in which articles 75 to 82 specifically cover "*research and experimentation*"[25].

"*Medical research involving a disadvantaged or vulnerable population or community is only justified if the research is responsive to the health needs and priorities of this population or community and if there is a reasonable likelihood that this population or community stands to benefit from the results of the research.*"[26]

There should be absolutely no possibility of violation of this general rule, formulated

19 John-Paul II, *Address of John Paul II to the Members of the Pontifical Academy for Life*, 24 February 2003.
http://www.vatican.va/holy_father/john_paul_ii/speeches/2003/february/documents/hf_jp-ii_spe_20030224_pont-acad-life_en.html

20 WMA (World Medical Association) *Ethical Principles for Research Involving Human Subjects*, commonly known as the *Declaration of Helsinki*
http://www.wma.net/en/30publications/10policies/b3/17c_en.pdf

21 Council of Europe (CoE), *Convention on Human Rights and Biomedicine*, Oviedo, 1997.
http://conventions.coe.int/treaty/en/treaties/html/164.htm

22 CoE, *Additional Protocol to the Convention on Human Rights and Biomedicine concerning Biomedical Research*, Strasbourg, 2005. This text will henceforth be mentioned as Additional Protocol.
http://conventions.coe.int/treaty/en/treaties/html/195.htm

23 CoE, *Additional Protocol to the Convention on Human Rights and Biomedicine*. This report will henceforth be mentioned as "*Explanatory Report*"
http://conventions.coe.int/Treaty/EN/Reports/Html/195.htm

24 International Ethical Guidelines for Biomedical Research Involving Human Subjects (WHO) Geneva 2002. This text will henceforth be mentioned as Guidelines, 2002
http://www.cioms.ch/publications/guidelines/guidelines_nov_2002_blurb.htm

25 The Pontifical Council for Health Pastoral Care, *The Charter for Health Care Workers*, 1995.
http://www.vatican.va/roman_curia/pontifical_councils/hlthwork/documents/rc_pc_hlthwork_doc_19950101_charter_en.html Cf. also Catechism of the Catholic Church, § 2295.

26 WMA, Helsinki Declaration 2008, § 17. http://www.wma.net/en/30publications/10policies/b3/

by the World Health Organization. Failure to comply with this rule would mean that the vulnerability of this population or community is being exploited to the benefit of other categories of persons. It would be contrary to the most basic rules for respecting human dignity and justice.

Vulnerability has many different aspects. Particular attention must be paid to it[27] when inviting a person to consent to participation in a clinical trial. However, specific rules may be set up regarding certain populations or groups of persons, particularly those who are not capable of expressing true informed consent; this includes the populations of countries where it is difficult for them to have proper understanding of clinical trials and their consequences, and where pressure could easily be applied, possibly in the form of offering some sort of gain.

27 Cf. Council of Europe, *Explanatory report*, § 69.

5. INDIVIDUALS INCAPABLE OF GIVING THEIR INFORMED CONSENT

According to international directives, persons coming under this category include minors and also adults who have been ruled as incapable by a court decision, and persons for whom it is impossible to be given adequate information or to express themselves due to their situation, either temporary or permanent.

Directive 2001/20/EC of the European Parliament and of the Council of 4 April 2001[28] clearly states: "*Persons who are incapable of giving legal consent to clinical trials should be given special protection*".

Obtaining the consent of research subjects is a fundamental imperative of research ethics. By definition, the objective of research consists in acquiring generalizable knowledge beyond individual specificities[29]. Thus, it does not focus on the good of the person. The consent of a person justifies that the person could – within certain limitations – be engaged in a clinical trial that does not completely respond to the person's own interests, and that the ratio between potential benefit and foreseeable risk might not be fully to that person's advantage. The person concerned may give consent for the good of others (and perhaps, later, in the person's own interest), in the "*medical interest of the community*", consequently for the "*common good*"[30], insofar as the person's physical and psychological integrity is not endangered. Such engagement cannot be imposed on the person.

Hence we derive the general principle that subjects of trials should not be sacrificed in the interests of science or the community of patients[31], and that every person engaged in a clinical trial must have given consent.

It is therefore only in some exceptional cases that approval can be given to research carried out on individuals incapable of giving their informed consent. Such research must be subject to the following principles:

"*Such persons may not be included in clinical trials if the same results can be obtained*

28 *Directive 2001/20/EC* Consideration 3.

29 Cf. CIOMS-WHO, *Guidelines*, 2002, Preamble.

30 Cf. PIUS XII, *Speech of 14 September 1952 on medical experimentation on human subjects* in*: Biology, Medicine and Ethics*, Paris, Le Centurion, coll. Les dossiers de la Documentation catholique, 1987, p. 219-229.

31 Ibid. See also Council of Europe, *Convention on Human Rights and Biomedicine*, Oviedo, 1997,art. 2.

using persons capable of giving consent"[32].

and

"*In medical research involving human subjects, the well-being of the individual research subject must take precedence over all other interests*"[33].

This paves the way for recommending a general rule governing clinical trials on medicinal products.

Trial medicinal products may only be administered to persons incapable of giving their consent in the event that the same results could not be obtained by resorting to persons capable of giving their consent and if the potential benefit and foreseeable risk ratio is to their advantage.

Furthermore, involving such persons in a research project will only be allowed if, in the aim of representing the interests of the person for lack of a consent that cannot be given, "*the necessary authorisation has been given specifically and in writing by the legal representative or an authority, person or body provided for by law*"[34] . The person will have been informed within his/her capacities and the research will not be carried out if the person expresses any form of opposition.

However, international institutions that tackle the issue of research carried out on groups of vulnerable individuals have nuanced their recommendations while calling for greater vigilance.

32 *Directive 2001/20/EC*, Consideration 3.

33 WMA, *Helsinki Declaration,* 2008, § 6. Cf. also CoE, Convention on Human Rights and Biomedicine, Oviedo, 1997, art. 2.

34 CoE, *Additional Protocol*, article 15.

6. CLINICAL TRIALS IN EMERGENCY SITUATIONS

There is a great deal of current debate on clinical trials in emergency situations. The possibility of using the adequate medicinal products when people's lives are endangered after a serious injury, or a sudden breakdown in health, allows many lives to be saved. We have seen this many times in the past few years. Research carried out in this area can thus – as long as people are handled with respect – represent a veritable life-saving service. However, the urgency of such situations makes it difficult, often impossible, to give full information to the patient, even more so when the initial shock or the severity of the breakdown in health widely affects his ability to understand or makes all his communication impossible.

Applying the abovementioned rules implies that the only specific research carried out on such patients might consist of trials for the care of persons in that situation and who could legitimately be expected to directly benefit from the research. In any case, the risk of such research must be minimal and only a minimal burden on the participants may be imposed, under the additional condition that the patient should not have previously expressed any reservation on the envisaged trial, and that, as soon as the patient is able to do so, he/she should be informed about the trial being carried out and give his/her consent to it[35].

The patient's consent can be reasonably presumed if all requirements – clearly listed in the proposed Regulation[36] – are fulfilled. A careful assessment of their application is indispensible when examining any clinical trial to be conducted in emergency situations. It would be advisable to add the authorisation of representatives of the persons concerned; these could be previously designated representatives or family members who could be contacted in time. To avoid any form of laxness that could ultimately lead to abusive situations, it is vital to give a sufficiently precise meaning of the terms "*minimal risk*" and "*minimal burden*". Several international

35 Cf. CoE, *Additional Protocol*, art. 19, § 3. "*Persons participating in the emergency research project or, if applicable, their representatives shall be provided with all the relevant information concerning their participation in the research project as soon as possible. Consent or authorization for continued participation shall be requested as soon as reasonably possible*".

36 *Proposal for a Regulation*, art. 32.

declarations[37] have covered this. The ethical committees called upon for verification that the persons included in research protocols are being duly respected and sufficiently protected must clearly demonstrate a high degree of vigilance and must refuse to give their approval to any project that would interpret these concepts of minimal risks and burdens too generously.

37 Cf. CoE, *Additional Protocol*, art. 17: 1 "*For the purposes of this Protocol it is deemed that the research bears a minimal risk if, having regard to the nature and scale of the intervention, it is to be expected that it will result, at the most, in a very slight and temporary negative impact on the health of the person concerned*". 17:2. "*It is deemed that it bears a minimal burden if it is to be expected that the discomfort will be, at the most, temporary and very slight for the person concerned. In assessing the burden for an individual, a person enjoying the special confidence of the person concerned shall assess the burden where appropriate*". Cf. also CIOMS-OMS, Guidelines 2002, n° 9.

7. RESEARCH CARRIED OUT IN DEVELOPING COUNTRIES

The questions raised by research carried out in developing countries have already been studied in two Opinions issued by the COMECE Reflexion Group on Bioethics[38]. The vulnerability of the population of several developing countries was emphasised.

"*…legislation provides less protection for people in the more developed countries.*

For the Secretariat of the Commission of the Bishops' Conferences of the European Union (COMECE) this situation gives rise to real concern. This is also the case for many institutions that work for the protection and respect of persons who are the subjects of biomedical research.

The populations of medically less advanced countries are far more vulnerable to proposals for experiments than in countries where medicine has advanced over several decades and where there are numerous sources of information. The very concept of research is foreign to them. This represents a major obstacle to providing adequate information. Consent is sometimes obtained by promising material benefits (or by applying psychological pressure), or even only on account of the prestige of the foreign investigators who have asked for their collaboration"[39].

The proposed Regulation only directly applies to research carried out in the European Union Member States. However, the pharmaceutical companies and universities of these countries do carry out research outside Europe, particularly in developing countries. Therefore, it is essential to recall the ethical demands relating to research carried out in these countries.

a) Respect of persons and populations engaged in this research and their access to research results

All biomedical research must respect the different cultural expressions in countries where research promoted and financed by institutions or enterprises from developed countries is carried out. These responsible institutions are not dispensed from respecting the values and fundamental rights that are recognised in their own

38 Cf. note 17.

39 COMECE, Science and Ethics, op. cit., "*Medical experiments*", p. 51.

countries.[40]

Respect for human dignity implies in particular:

- that a person must not be reduced to the status of an object for research;

- that no act on the human body may be carried out without having first obtained the true consent - free and informed - of the person on whom the research is to be conducted. This does not exclude, according to the various cultures, different ways of obtaining the consent, nor dialogue with the authorised representatives of the person and of the community concerned;

- that financial or other incentives, which represent a form of commercialisation of the body, are excluded;

- that the requirements of justice should be scrupulously respected which would require from the sponsor and the investigators that they ensure that the research is responsive to the health needs and the priorities of the population or community in which it is to be carried out; and that any intervention or product developed, or knowledge thereby generated, will be made reasonably available for the benefit of that population or community[41].

"*It is indeed appropriate to make sure that the community, in which the experiment has been undertaken, benefits from it and that, as general rule, the local population has access to any medical developments that may result from the trials*"[42].

Carrying out research creates a bond of responsibility between the sponsors of the clinical trial and the host countries and the persons submitting to the research. "*The promoters cannot disregard, directly or indirectly, the future of the person that they have recruited to be the subject of the research. This implies that they must engage in advance in order to ensure that if there is a positive trial result then they should benefit from this; and to take appropriate measures if the research has had negative consequences or creates risks for those who have undergone treatment in the trial. In any event, the promoters will have to enable members of the community concerned to participate actively in the research, so as to achieve a dissemination of*

40 Cf. COMECE, *Science and Ethics*, op. cit., "*Biomedical research in developing countries*", p. 45. Cf. also: CIOMS-WHO, Guidelines 2002, Introduction.

41 Cf. COMECE, *Science and Ethics*, op. cit., "*Biomedical research in developing countries*", p. 45. Cf. also CIOMS-WHO, Guidelines, 2002, Guideline 10.

42 Cf. COMECE, *Science and Ethics*, op. cit., "*Biomedical research in developing countries*", p. 46.

knowledge and know-how"[43].

"*The ethical requirement that research be responsive to the health needs of the population or community in which it is carried out calls for decisions on what is needed to fulfil the requirement. It is not sufficient simply to determine that a disease is prevalent in the population and that new or further research is needed: the ethical requirement of «responsiveness» can be fulfilled only if successful interventions or other kinds of health benefit are made available to the population. This is applicable especially to research conducted in countries where governments lack the resources to make such products or benefits widely available*"[44].

In view of the extent of the interests at play, there is a lot of debate on whether trial results should be made available to people having participated in the research and their community. But refusal to recognise such demands would mean using populations for ends unrelated to them and would thus represent a form of exploitation of vulnerable populations that is in direct contradiction with the general principle that should govern any research involving such populations[45].

b)The duty of solidarity towards health-deprived populations

This requirement of respect of the populations of poorer countries must not obscure the duty of solidarity that consists, for developed countries and their institutions, in participating to the fight against endemic illnesses affecting millions of persons in developing countries. For many such diseases, it is urgent to launch or develop research that will lead to the invention of adequate prevention or treatment means of these illnesses. Dr Margaret Chan, Director General of the World Health Organisation (WHO), recently stated: "*expediting the development of new medicines, diagnostics, and vaccines for the neglected tropical diseases, malaria, and tuberculosis*"[46]. The Director General of the WHO continued in these terms:

"T*he demand for such products is huge, as this group of diseases affects more than one billion people. As we all know, market forces fail to drive innovation because this particular market has virtually no capacity to pay. Any price, when multiplied by the*

43 Ibidem p 46.

44 CIOMS-WHO, *Guidelines*, op. cit., Guideline 10.

45 This principle is laid down in § 17 of the aforementioned *Helsinki Declaration*. Cf. note 26.

46 Dr Margaret CHAN, *Launch of innovative research and development consortium for neglected tropical diseases, malaria and tuberculosis*, 26 October 2011,
http://www.who.int/dg/speeches/2011/innovative_research_26_10/en/index.html

millions, is too high for the bottom billion to pay […].

Despite the numbers affected, the neglected tropical diseases usually fall below the radar screen of priority health problems.

These are not diseases that travel widely or threaten more affluent groups. They stay put in areas where housing is substandard, safe water and sanitation are scarce, environments are filthy, and disease-carrying insects and animals are abundant. […]

Let me encourage the members and supporters of this [newly created] consortium to make the goals of affordability and accessibility central to your work as new products are developed. Health officials in the developing world tell me time and time again: a vaccine that is too expensive is worse than no vaccine at all.

Equally important is to respect the strong desire, in developing countries, for assistance that helps them build their own R&D capacity to manage their own priority diseases and health needs"[47].

The duty not to carry out clinical trials in developing countries that would de facto only benefit populations of developed countries should not thus become an alibi to discontinue conducting any sort of biomedical research or clinical trials on these populations.

As for many other ethical issues, it is essential to find a balance between two groups of requirements that seem to contradict each other: on the one hand, not taking advantage of the vulnerability of some populations to exploit them as subjects to experiment on and, on the other hand, to demonstrate a spirit of initiative to launch the research programmes that these countries need and find the necessary financing. If the industrial and commercial sector is not best suited to this task because of "*market laws*", other paths must be found by calling on the resources of Member States and of the major humanitarian organisations. The European Union cannot stand aloof from the dramatic scenario of diseases that are so widespread yet mainly left without any cure.

The huge and urgent needs of health-deprived countries require debate. Another way of organising research has to be found which would be less profit-oriented and would be run in developed societies much more along lines of realisation of their responsibilities and a spirit of solidarity with resource-poor populations.

"*It is essential to realize that to leave these peoples without the resources of science*

47 Ibidem.

and culture means to condemn them to poverty, financial exploitation and the lack of health care structures, and also to commit an injustice and fuel a long term threat for the globalized world. To value endogenous human resources [of these countries] means to guarantee the balance of health care and, in short, to contribute to the peace of the whole world. Thus the relevant moral dimension of biomedical scientific research necessarily opens to the dimension of justice and international solidarity"[48].

48 John-Paul II, *Address of John Paul II to the Members of the Pontifical Academy for Life*, 24 February 2003, op.cit. (cf. note 19), § 6.
http://www.vatican.va/holy_father/john_paul_ii/speeches/2003/february/documents/hf_jp-ii_spe_20030224_pont-acad-life_en.html

8. A BROAD SCOPE OF ASSESSMENT

Clinical trials on medicinal products thus raise innumerable ethical questions that have been the subject of international declarations, recommendations and conventions from which the European Union largely drew inspiration for its Proposal for a Regulation. The Charter of Fundamental Rights of the European Union adds to this. Every research project must be assessed from an ethical perspective using this wealth of reference documents. The area of responsibility of the bodies responsible for this assessment within each Member State is huge. The currently proposed Regulation presents limitations on, first of all, the very tight deadlines granted for assessments. It is absolutely vital that these limitations should not pose obstacles to a calm in-depth examination that would ensure that clinical trials on medicinal products are geared toward serving the various categories of patients in the complete respect of the persons and populations upon whom such trials are conducted.

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