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Preimplantation Genetic Diagnosis

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Contents

Summary

In its Opinion no. 10/2005, the Swiss National Advisory Commission on Biomedical Ethics (NEK-CNE) presents detailed ethical arguments and recommendations for the regulation of preimplantation genetic diagnosis (PGD). A majority of the Commission recommends that the existing wholesale ban on PGD should be replaced by restricted legalization, with an indication-based approach.

According to these recommendations, PGD should be permitted for couples known to be at risk of transmitting a serious hereditary disease to their offspring. Equally, PGD should be permissible for couples undergoing in vitro fertilization (IVF) for the treatment of infertility. Eugenic practices of all kinds are, however, to be ruled out. The Commission also recommends prohibiting PGD for the purpose of embryo selection based on immunological characteristics, designed to provide cells for the treatment of an existing sibling. A minority of the NEK-CNE recommends that the complete ban on PGD should be maintained.

Under the Reproductive Medicine Act (FmedG), which has been in force since 2001, PGD is currently prohibited in Switzerland. The reasons that led to the imposition of this ban have been considered by the NEK-CNE. The conclusion reached by a majority of the Commission is that, while concerns are rightly expressed about eugenic practices, these can be better addressed through regulations involving clearly specified indications. The key ethical objection to the existing ban is the paradox that arises for couples with known genetic risks: although they are currently allowed to embark on a «trial» pregnancy, which may possibly be terminated after prenatal diagnosis (PD), tests are not allowed to be performed on the embryo before it is transferred to the womb. For the majority of the Commission, it is not clear why it should not be possible for an IVF embryo to be tested for serious genetic diseases prior to transfer, while a fetus at a much later stage of development can be subjected to prenatal diagnosis, possibly followed by a termination of pregnancy.

Under the Commission's proposals, PGD should also be permissible for couples undergoing IVF treatment, in order to exclude chromosomal anomalies that would impede or prevent embryo development. In view of the eugenics argument, however, the majority of the Commission recommends that PGD should be prohibited in all other cases, particularly for embryo selection based on non-disease-related characteristics, desired traits or even sex.

A minority of the Commission wishes to see the existing ban on PGD maintained, noting that the procedure always involves selection of embryos, which it considers to be incompatible with human dignity as a fundamental value. In addition, for this minority, there is no guarantee that PGD, together with PD, will not in fact lead to discrimination against children with disabilities.

Chapter III: Questions considered by the NEK-CNE

3.1 Serious hereditary diseases: the central concern

The Working Group's deliberations were guided by the problems that arise in practice. Of central concern are situations where there seem to be particularly good reasons for permitting preimplantation genetic diagnosis (PGD). Reference to such situations has also been made on various occasions in the political debate. Such situations give rise to an intuitive sense that PGD could be indicated, namely when there is a high risk that a couple's offspring will suffer from a serious hereditary disease.

A typical example : Mrs K has given birth to her first child, which after only a few weeks develops a form of muscular atrophy known as Werdnig-Hoffmann disease, with an extremely poor prognosis; the infant rapidly weakens and soon dies. The despairing parents are informed about the «retention of samples for future use», but in their grief they do not grasp the significance of this «future» use. Several months after the child's death, the mother becomes pregnant again. The couple inquires about the possibility of prenatal diagnosis (PD) and is referred to the Medical Genetics Department of the University Hospital. Here, they are told that PD can be carried out by analysing the retained tissue sample from the first child. The DNA analysis confirms that the first child had suffered from Werdnig-Hoffmann disease, and unfortunately a chorionic villus biopsy indicates that the developing fetus will also be affected. The parents decide to terminate the pregnancy. On the Internet, they discover that in such circumstances it would be possible to perform PGD after in vitro fertilization (IVF) and to select from a number of fertilized egg cells one that is not affected by the disease. However, as their gynaecologist points out, this procedure is prohibited in Switzerland. The parents consider travelling to Belgium for this purpose – to Brussels University Hospital – where the procedure is permissible and available for this indication. They are aware that they will have to bear the costs themselves.

In a situation of this kind, it is difficult to comprehend why prenatal diagnosis followed by termination of pregnancy should be allowed while at the same time it is forbidden to carry out a test that would make it possible to determine after IVF whether or not the embryo is a carrier of the disease. This is paradoxical. With PGD, the woman could be spared the experience of a «trial» pregnancy (trusting to luck, as it were) and a possible termination. Many people would consider it more humane to allow an embryo to die at a very early stage – in the first few days after fertilization, before a pregnancy has even been established – than to end the life of a more fully developed embryo or fetus in the third or fourth month of pregnancy. In cases of this type, at least, it is not clear why the law should prohibit the use of PGD, if it can be performed sufficiently safely.

In its deliberations, the Commission assumed there to be a discrepancy between two legal norms. In addition, it considers that efforts to help shape the genetic fate of offspring can be supported on ethical grounds if it is possible to prevent the occurrence of serious diseases. Accordingly, legalization of PGD would not only be a matter of justice, given that the option of PD is already available, but also an appropriate medical measure as such. However, the Commission concluded that the implications still need to be carefully considered before any change in the law can be recommended. Although the series of objections raised in the debate on the legalization of PGD do not call into question the ethical intuition itself, they do in-

[1] Based on Guido de Wert, Ruud ter Meulen, Roberto Mordacci and Mariachiara Tallacchini: Ethics and Genetics. A Workbook for Practitioners and Students. New York/Oxford: Berghahn 2003, pp. 27f. "The case of Peter and Karin".

dicate direct and indirect disadvantages or risks for individuals and society that would have to be accepted even if the practice were to be legalized with certain restrictions. The opponents also point out that the dilemma only arises if two crucial presuppositions are made, namely that the couple in question should have a child that is genetically their own and that a sick child is a «misfortune», a burden difficult to bear. They argue that alternative methods of helping the couple to become parents are available – oocyte or sperm donation, or adoption. Finally, they point out that to forgo children of one's own is an option which is no longer subject to disapproval in today's society.

3.2 Discussion of fundamental objections

3.2.1 Reasons for the prohibition of PGD in Switzerland

The legal framework for the prohibition of PGD in the Reproductive Medicine Act (FmedG, in force since 1 January 2001) differs from that in Germany inasmuch as Switzerland does not have a specific Embryo Protection Act, although certain prohibitions regarding the handling of embryos are enshrined in the Swiss Federal Constitution, as well as in legislation. For example, the cloning or commercialization of embryos is prohibited, as is embryo donation. In the Federal Council's Report on the FmedG, the following reasons were given for imposing a ban on PGD (as discussed in Section 2.4 above):

1. The long-term consequences for the embryo tested are unknown.
2. The possibility of misdiagnosis exists.
3. There is a serious risk of embryo selection becoming ever more widespread.
4. It is impossible to draw a borderline between prevention and selection.
5. There is a risk of certain findings automatically leading to selection.

Crucially, the ban on PGD not only covers totipotent embryonic cells but is applicable in a general manner. Thus, Art. 5, Para. 3 of the FmedG states succinctly and unequivocally: «The removal and investigation of one or more cells from an embryo in vitro is prohibited». In contrast to the question of moral status that dominates the debate in Germany, the arguments underlying this prohibition are of a consequentialist nature; i.e. they do not involve the ascription of a characteristic such as human dignity to a zygote or an embryo but are based on consideration of the consequences that a given course of action could have.

From the perspective of the above-mentioned case of serious hereditary diseases, the following comments may be made in response to the reasons enumerated above:

1. It must remain clear that there can be no guarantee of complete safety with PGD. Those concerned are exposed to a certain long-term risk of an unknown qualitative and quantitative nature. However, this does not set PGD apart from other novel or conventional medical measures. It gives rise to, firstly, a duty of care and a requirement for quality assurance in the management of the technologies applied and, secondly, the need to ensure that PGD is only used for medical reasons. But it does not necessarily provide grounds for a ban.
2. There is a possibility of misdiagnosis, i.e. either false-positive or false-negative results. However, once again, this does not make PGD any different from PD. With a false-positive diagnosis, the transfer of a healthy embryo does not occur, but equally no sick child is born as a result. In the event of a false-negative diagnosis, an affected embryo may be implanted, but this would also be possible with natural fertilization in the absence of PGD. If the results of a test are too uncertain, one could consider offering PD for verification purposes.

3. PGD is a method of selecting embryos according to genetic criteria. Within an IVF cycle, the procedure makes it possible to prevent the development of those embryos that are carriers of a given disease. However, the question arises of the ethical significance that should be attached to the selective aspect. It should be borne in mind that the selection of embryos in the presence of a known risk of disease within an IVF cycle is not the same as the selection of members of society according to desirable and undesirable characteristics. There are also fears that the practice of selection would become increasingly widespread. This «slippery slope» argument suggests that once the method is legalized, it would no longer be possible to prevent the extension of its applications. In response, it may be asked why it should not be considered possible to prevent PGD from being extended to illegitimate applications (e.g. sex selection) with the aid of appropriate regulations. Our entire legal system is based on the premise that clearly defined legal prohibitions – even though they may be breached in individual cases, triggering sanctions – are still an appropriate instrument for steering behaviour in a socially desirable direction.
4. The impossibility of drawing a borderline between prevention and selection is not to be dismissed, inasmuch as PGD always involves selection of IVF embryos. At the same time, it also replaces the selection of embryos and fetuses at a more advanced stage of development, representing a choice of the lesser of two evils. The drawing of the borderline can be guided by this idea of replacing an even less satisfactory alternative.
5. The risk of certain findings automatically leading to selection also attaches to PD. Thus, this objection does not apply merely to PGD. However, opponents further point out that in the case of an established pregnancy the ties existing between the woman and the fetus give rise to an emotional conflict which means that a termination of pregnancy will not be undertaken lightly. In contrast, a pre-planned decision not to transfer an embryo could as a rule be implemented without any such conflict. It is argued that, while PD involves a concrete conflict between the right to life of the embryo or fetus and the woman's interests (cf. Section 2.1.1.), no such conflict of interests arises with PGD; instead, this procedure is concerned with the woman's or couple's plans for the future and with the creation of «selectable» embryos. On the other hand, it may be asked what right society has to force a woman into this kind of conflict of interests, with all the risks and burdens associated with a termination, if a pregnancy with an affected embryo could be averted altogether.

On reviewing the five ethical arguments used to justify the general ban on PGD in Switzerland, not one of them can be found to rule out the possibility of restricted legalization in an unequivocal manner, without an equally plausible opposing position. However, the arguments do highlight a series of risks for the individual and society which need to be addressed preventively in legal regulations.

The goal that could serve to legitimize the use of PGD is that of replacing some of the prenatal diagnostic measures undertaken during pregnancy which may lead to a termination. This replacement would consist of measures that can be taken in the laboratory following IVF and which, in the event of abnormal findings, would lead to a decision to forgo the establishment of a pregnancy and to allow the embryo to die. The aim is thus primarily to spare women the painful experience of PD with a subsequent termination, and to offer them the option of a pregnancy that is as far as possible risk-free from the outset. PGD does, however, always require an IVF procedure, which in itself imposes certain physical and psychological burdens.

One difference, also emphasized within the Commission, concerns the level of protection afforded to an embryo, depending on whether it is «exposed» in a laboratory vessel or physically «protected» within the mother's body. In the case of pregnancy, the embryo already enjoys special protection merely on account of the physical and emotional ties existing between

it and the mother. However, it cannot be maintained that an embryo in vitro enjoys no protection whatsoever – after all, it was deliberately created as a result of the parents' desire for offspring.

What objections – beyond the attribution of a moral status that would render the embryo inviolable – could be raised against PGD that have not already been raised against PD – without the latter having been repudiated by society as a result? This question is important for the assessment of PGD since one of the main arguments advanced in support of the procedure is that it is to be seen as an «early-stage» PD, offering the possibility of reducing the number of terminations following PD during pregnancy.

One major difference between the two types of procedure appears to lie in the fact that PD involves an additional physical relationship to the fetus (pregnancy) – a relationship that does not yet exist at the time of PGD. However, IVF already involves a kind of visual diagnosis: embryos are inspected under the microscope and only the regular, «well-developed» embryos are chosen. The «poorly developed» embryo of irregular morphology is not transferred to the patient's womb. In contrast, PGD is an invasive diagnostic method – how great a «qualitative leap» should this be considered to involve?

3.2.2 Social conditions underlying autonomy

Reproductive medicine has developed within a complex social environment and, like other advances in the field of medical technology, it has been the subject of controversy. For its supporters, the concept of «reproductive autonomy» (as discussed in Section 2.2.2.) is central: on this view, the decision whether or not to undergo a given intervention is a matter for those concerned. Opponents, however, raise the question of whether reproductive medicine meets the demands of the woman's or couple's enlightened autonomy, or whether it does not rather serve the principle of performance extended so as to cover even the spheres of sexuality and reproduction («the body is required to function»)? They argue that while PGD expands the options available for controlling reproduction, it also increases the pressure to produce offspring «complying with standards». Genuine freedom would require the two alternatives to be accorded equal status, but this is not the case given the constellation of authorities and the general conditions for families and also in view of cultural influences. From the perspective of society as a whole, a liberal form of eugenics could be established in the name of self-determination, with women's autonomous decisions being influenced by society's pursuit of normalization; this would call autonomous decision-making into question. The ethical debate is thus also concerned with the question of whether the new kinds of interventions should be considered in terms of an increase in reproductive autonomy or rather in terms of forced decisions.

Increased freedom and autonomy also involves an increase in responsibility. This gives rise to a further objection against the reproductive autonomy argument: if individuals fail to adapt to the requirements of modern societies, they will be personally blamed. If a couple freely decides not to make use of PGD in the face of a genetic risk, it will have to take responsibility for the outcome of this decision, i.e. possibly for their offspring suffering an avoidable tragic fate.

The Commission acknowledges the legitimate concern underlying this objection. It believes that this concern needs to be taken into account in the further development of the social framework. At the same time, similar objections also apply to PD. In other words, PGD is not liable to the objections raised against reproductive autonomy if it can already be assumed that PD is to be performed. If society has decided to enable women to have their fetus investigated prenatally, the resultant moral conflicts or social problems do not provide any grounds for banning testing of the embryo before the onset of pregnancy.

3.2.3 Selection

As long as treatment options remain unavailable for certain diseases, the purpose of any kind of embryo diagnosis is to perform «selection», thereby preventing the development of children that would suffer from the diseases in question. This is true irrespective of the developmental stage of the embryo at the time of diagnosis and whether testing is carried out in vitro or in vivo. As in the debate on PD, fears have been expressed that this type of selection calls into question the value of the life of people with disabilities. While the NEK-CNE understands these concerns, it considers respect for the disabled to be independent of a ban on PGD. Legalization of PGD does not in itself entail any decrease in respect for the disabled.

The use of both PD and PGD only makes sense if one knows what one is looking for. Molecular genetic studies can be applied particularly in cases where a pathogenic gene mutation has already been diagnosed in the parents or in a sibling. With the aid of new technologies, it has been possible to bring forward the time of selection to ever-earlier stages.

Selection – «choosing» among different embryos – is only possible with an IVF procedure. The aim is to screen the embryo for genes or chromosome aberrations known to cause specific diseases or disabilities. With regard to «selection», it is important to note that a woman is scarcely likely to undergo the onerous IVF procedure voluntarily merely in order to select an embryo according to non-health-related criteria. For the mother, the procedures that make «selection» possible are physically and psychologically burdensome.

There are differences between PD and PGD concerning the way in which decisions are taken. A decision about a termination of pregnancy following PD is taken by the woman or couple with the support of the physician. The time available for this decision is limited, but still longer than in the case of PGD. In addition to the burdens imposed by a termination, there is the moral stress associated with the selection decision. In contrast, the decision concerning non-transfer of an affected embryo following PGD is taken by the physician, together with the couple, very shortly after the diagnosis has been made. In this case, the physical and psychological stresses of the IVF procedure represent the main burden for the mother, rather than the decision on selection, and the burden of a termination is absent.

3.2.4 Risks of extension of indications

Although the risk of embryo selection becoming ever-more widespread cannot be used to justify a ban on PGD, the possible extension of early genetic screening needs to be taken into account in any nuanced legal regulations. The fact that a slippery slope is already associated with PD does not mean that it is not important in relation to PGD. The following points were discussed by the Commission:

- Criteria other than what a woman can be reasonably expected to accept (the so-called maternal indication) will come to be considered; greater weight will be attached to the woman's desire to have a child free of disease/disability.
- Requests could also be made concerning any risks detectable by genetic testing, aesthetic characteristics, or even the sex of a child. A law would thus be required to establish a clear framework. However, rather than pre-empting all decisions, the law should also take into consideration the fact that genetic counselling enables decisions to be weighed up together with those concerned in individual cases.
- A right of defence (not being required to embark on or continue with a pregnancy) could become an entitlement (to have a healthy embryo).
- Reproductive medicine can be used for prevention of disease. With its assistance, parents can fulfil their responsibility for the health of their offspring. This creates a need for the definition of limits, so that it does not give rise to social eugenics for the purposes of population policy.

- PGD could become part of the «standard package» of IVF services, since from a medical perspective it would be ethically questionable not to offer an available procedure of proven value that could prevent the transfer of an embryo foreseeably or even possibly affected by disease.
- In the face of this social and medical pressure, is it possible with the aid of a law to maintain a woman's freedom to decide? Even if this freedom (as in the case of PD) is subject to certain strains, it is better to have legal regulations specifying that no pressure is to be exerted on the woman, and that the couple's decision is to be supported by the provision of high-quality counselling which covers the genetic, medical, ethical and psychosocial aspects.
- Society needs to address the risk of extension through a clearly formulated law. However, infringements or abuses cannot be prevented by any law or ban. The possibility of abuse does not force us to prohibit the legitimate use of a method (abusus non tollit usum)
- The existence of a ban in Switzerland forces affected couples to seek assistance at centres abroad. Here, too, abuses may occur. In addition, the quality of treatment abroad varies.

3.2.5 Risks of IVF for the woman and child

Factors possibly arguing against relaxation of the ban on PGD include the burdens and risks arising for women from the IVF procedure following hormonal stimulation of the ovaries and follicular aspiration. It is known that after IVF some women develop a severe form of ovarian hyperstimulation syndrome (cf. Section 1.5.). In addition, the emotional strains of IVF for women and men are well known. Nonetheless, in some infertile couples the desire for children is so strong that women and couples knowingly assume these burdens and risks. If an IVF procedure is to be carried out anyway, i.e. in the case of infertility, consideration would need to be given at most to the additional risk of complications which arises from the fact that more oocytes are generally extracted for PGD than with «conventional» IVF. The question of risks and burdens deserves particularly serious consideration in those cases where IVF would not otherwise be performed. This applies to couples with a genetic risk who are, however, fertile.

For certain types of male factor infertility, intracytoplasmic sperm injection (ICSI) is now an established method. Another question that needs to be discussed, therefore, is whether IVF, possibly in combination with ICSI, poses risks for the fetus or child. IVF involves an increased probability of multiple pregnancy, which in turn (as explained in Section 1.2.1.) carries a risk of disease for the children concerned. On the other hand, the likelihood of pregnancy in a given cycle decreases with the number of embryos transferred. There is, however, also evidence (cf. Section 1.2.1) to suggest that IVF and ICSI also increases the risk of malformations and harmful peri- or postnatal complications in the case of singletons. For this reason, there is a trend towards fewer embryos per cycle – in Switzerland two embryos are currently transferred in IVF procedures. The long-term effects of embryo biopsy for the child are not yet known, as very little empirical data is available to date. The viability of the embryos (as explained in Section 1.4.2.) is not significantly affected by this intervention. Despite detectable delays in development following embryo biopsy, the proportion of embryos developing into blastocysts remains unchanged.

The health risks for the child that are associated with assisted reproduction, which obviously cannot be dismissed, provide substantial ethical grounds for only performing IVF and ICSI in cases where even greater risks or burdens can thereby be averted or where, as a result of infertility, procreation would not otherwise be possible. PGD has to be justified by the risk of a serious genetic disorder. In addition, the Commission is concerned to ensure that, when couples decide whether a reproductive medical measure is to be carried out, they are openly and fully informed about the associated risks and burdens both for the woman and in particular for the child.

3.3 Overview of possible indications

In the debate on situations of different types, a simple, schematic classification has proved valuable. This is based on the perspective of the couple concerned. The woman and the man may possibly already know that they have a given likelihood of being carriers of a genetic disease. These couples may additionally – possibly as a result of this carrier status – be infertile and therefore have recourse to assisted reproductive techniques. Couples with no known risk for transmission of a genetic disease may likewise be fertile or infertile. In the case of infertile couples that may resort to IVF, there are good grounds for considering separately those women who on account of their age have an increased risk of chromosomal anomalies. For the sake of completeness, mention should also be made of situations in which PGD is used to select a child that could provide stem cells for an existing sick sibling (the so-called bébé médicament or designer baby, see section 3.6). The following basic scheme can thus be applied:

1. Couples have been shown to be carriers of a serious hereditary disease
   a. fertile: dilemma, as PGD additionally requires IVF
   b. infertile: IVF is already being performed
2. Couples have no known genetic risk and are
   a. fertile
   b. infertile:
      I. prenatal diagnosis (PD) is indicated on account of the woman's age
      II. younger women with no increased risk of chromosomal anomalies
3. Selection of an embryo in order to permit treatment of an existing child

The «infertile» women include those who have previously undergone sterilization on account of a genetic predisposition (secondary infertility).

3.4 Parents who are carriers of diagnosable hereditary diseases

The option of PGD with embryo biopsy seems to be particularly suitable for infertile carriers of diagnosable conditions. It could be asked, more pointedly, is it even ethically justifiable in such cases for a pregnancy to be established with an embryo that has not been genetically screened, if it is known that this would subsequently involve PD and a possible termination?

The group of carriers of diagnosable conditions includes the above-mentioned couples with our «central indication» – parents at high familial risk of having a child with a serious hereditary disease. This is the case, for example, if they are both carriers of Tay-Sachs disease, Duchenne muscular dystrophy, cystic fibrosis, etc. Unless these couples decide to forgo children or to make use of gamete donation, they will face the prospect of PD and a possible termination.

However, there are also good arguments for including in this group couples with an increased risk for the occurrence of developmental disorders during pregnancy. Also to be included are parents who have reason to fear that the fetus will not develop to term or that the child will be born with a serious congenital condition. This is the case, for example, if one parent exhibits a balanced chromosome translocation. Likewise affected are parents at high risk of passing on a chromosomal disorder leading to developmental disorders. The two indications IVF and treatment of an existing child are discussed separately below.

3.5 IVF for infertility as an indication for PGD

Should PGD be made available as part of an IVF procedure for infertile women over 35 at increased risk for chromosomal aberrations on account of their age, since they would also be offered the option of PD anyway?

This question, which concerns an additional indication, was discussed in depth by the Commission. As noted in Section 1.3., about 70% of IVF embryos exhibit chromosomal anomalies and hence do not lead to pregnancy. This is also the case for healthy couples and does not apply only to older women. PGD could substantially increase the low success rates of IVF (as measured by the establishment of pregnancy).

The Commission discussed the question of whether the use of PGD to increase the efficiency of IVF is desirable and how this is to be assessed ethically. It concludes that it is very difficult to find compelling arguments against the provision of PGD for this indication. There is, however, one weighty ethical argument in favour of such provision: briefly, it is that if something is worth doing, it is worth doing well. IVF is an onerous procedure, involving slight but demonstrable risks for the mother and child. It is therefore a requirement of medical ethics to use the available options to make the procedure safer. This entails further development of the procedure, as gauged by the health of the woman and the resultant child. PGD could make a very important contribution to this process. However, a series of concerns have been raised:

1. If PGD were offered together with IVF to increase its efficiency, decisions could no longer be taken on an individual basis; although legally the woman concerned would always be guaranteed the option of declining PGD, she might not in practice be in a position to decide against it. However, it may be objected that this argument does not essentially militate against PGD in this indication; instead, it suggests that the woman must be given the possibility of making an informed and explicit decision. The «multipack» objection, though legitimate, does not argue against PGD in association with IVF; it provides a reason for ensuring that a decision to make use of PGD is not a matter of routine.
2. It needs to be asked whether it is not dangerous to permit PGD in this indication for healthy but infertile couples, since it would then also have to be permitted for other indications involving an increased risk beyond the «central indication» and ultimately could not be restricted. Underlying this concern is the fear of the spread of a «liberal» form of eugenics, accentuating the trend towards the standardized body. Even if one accepts the validity of this concern, it may be replied that it could be addressed by calling for clear legal provisions to protect the diversity of forms taken by the human body and to guarantee that testing remains voluntary. At the same time, it should be ensured that social conditions are such that the birth of a child with a disease or disability represents a possible prospect for the parents. The incidence of births of children with a disease or disability can only be influenced to a minor extent by the further spread of preimplantation and prenatal testing.
3. Concerns have been expressed that screening for individual characteristics could be offered, and that this could give rise to an obligation to participate in such screening. The Commission takes a highly sceptical view of the idea of screening as part of PGD and attaches great importance to the possibility of decision-making in individual cases. At any rate, screening could never be permitted without the couple's voluntary informed consent.

3.6 Selection for therapeutic purposes for the benefit of a third party

Should it become an option for a child to be conceived in the hope that it may serve as a donor of haematopoietic stem cells (or other cells) for a sick sibling? A frequently discussed example is that of Fanconi anaemia. In principle, the PGD technique would allow HLA typing to be performed so that immunocompatible donors could be identified. This application of PGD is clearly designed to benefit a third party, the aim being to cure an existing child that is seriously ill. The new child itself is not harmed by this procedure (apart from the burden of a bone marrow biopsy in early childhood). While supporters of this idea do not see any ethical objections in principle, they recognize the potential problems concerning the conditions for its application and draw attention to the question of how eligible recipients are to be defined. For example, should the possibility of donation for the benefit of sick parents also be considered? Would donation outside the nuclear family be permissible?

The terms used to describe such cases, especially in the media, are misleading. If one speaks of a «designer baby», one elevates the act of selection into an act of creation, with overtones of human breeding. The «bébé médicament» suggests a (positive) medical-ethical evaluation, but at the same time implies that the child is reduced to a mere (therapeutic) agent. The term «saviour baby» is explicitly euphemistic and evokes the moral context of emergency aid or salvation. If the ethical aspects of this potential constellation are to be elaborated in an unbiased manner, it is therefore necessary to avoid these formulations. Judgments should not be formed on the basis of the implications of these terms. In order to assess the actual issue, one needs to consider the following problematic aspects in particular:

1. A child is being created for a particular purpose
2. A child is being used as a therapeutic agent (instrumentalization)
3. The physical integrity of the child, which cannot yet give its consent, is breached, with the attribution of an altruistic attitude
4. Healthy embryos are rejected in the selection process
5. It is difficult to define limits
6. Strategically, alternative options exist.

In a detailed consideration, the following points may be emphasized:

As regards 1): From a parental perspective, the creation of offspring for a particular purpose may be ethically problematic. However, this is not an unusual occurrence in everyday life: for example, a father or mother may wish to have an heir for their business or farm, or someone to look after them in their old age, etc. Even in such cases, however, the parent-child relationship is not reducible to this purpose-related aspect. It remains possible for the child to become an independent individual with (or contrary to) these parental hopes. This will certainly also depend on the individual circumstances, and especially on the way in which these hopes are discussed within the family. The creation of offspring for a specific purpose by natural means cannot otherwise be prohibited; prohibition is only possible in this case because a special technique of a new kind is involved. At the same time, arguments in favour of PGD were also considered by the Commission: must the gravely ill child – the question was raised in the Commission – first be allowed to die before one is allowed to create another child that would offer the prospect of treatment? What is reprehensible about combining the hope of an advantage for the first child with the creation of a second child?

As regards 2): Instrumentalization would provide ethical grounds for ruling out the procedure if it were complete. According to Kant's categorical imperative, other people are always also to be treated as ends in themselves and never merely as means. In many relationships within the social division of labour, we treat other people performing a service for us as means for the performance of this service. The crucial point, however, is that we do not reduce them to this function of being at our service. We must always, as Kant said, also treat their humanity as an end in itself. It is not to be supposed that parents who decide to apply PGD in the context of therapeutic selection for the benefit of a third party wish to have the child merely as a means to this end. To make this imputation could well be to do their moral sensibilities an injustice.

As regards 3): At the time of donation, the child cannot give its consent. The parents are required to give their consent on the child's behalf, while safeguarding its interests. The ethical difficulty lies in the fact that the child itself has no interest in the intervention. The parents therefore have to credit the child with an altruistic altitude, anticipating that it would, if it could, consent to the donation out of love or solidarity with its sibling. In addition, it is not appropriate to speak of a «donation» when what is involved is the removal of cells from the child without its consent (and even contrary to its current interests), using a procedure that is invasive and not painless.

As regards 4): The ethical assessment of selection in this context has to take account of one particular element: in the process of identifying traits with no bearing on the health of the future child itself (and not relating to disease in the embryos screened out), certain embryos would be singled out and the others rejected. A selection practice of this kind, however, is felt by many members of the Commission to be morally offensive and considered to be ethically reprehensible.

As regards 5): It would be difficult to find convincing grounds for restricting the legalization of therapeutic embryo selection by PGD for the benefit of a third party to the «index case» of Fanconi anaemia. Other serious diseases of childhood that are treatable by the donation of immunocompatible haematopoietic stem cells could scarcely be handled differently. The question of who should be eligible as a recipient also arises. Are there sufficient convincing grounds for restricting application of this procedure to siblings? Why could more distant relatives not also be treated? Or parents, in whose health the child would have an even greater interest? It is also unclear on what convincing grounds donations could legitimately be restricted to haematopoietic stem cells. Why could cells or tissues of other types not also be donated – for example, a kidney or part of the intestine?

As regards 6): There is a need to investigate whether, from a strategic viewpoint, the use of PGD for the selection of a possible «donor» is actually the only therapeutic option available. The development of public cord blood banks, for example, also offers an opportunity to obtain suitable, HLA-matched haematopoietic stem cells for transplantation. From the perspective of parents living in the «here and now», however, PGD may in fact represent the only option. For such parents, and for situation ethics, this may even provide a decisive and ethically respectable reason for having this procedure performed at a foreign centre, where it is legal. The strategic view is, however, more appropriate for discussions of the shaping of future legislation.

3.7 Polar body biopsy

One point to be considered in the forthcoming decision on legislation is whether polar body biopsy (PBB) is ethically preferable to PGD and should therefore be supported. Compared with PGD using embryo biopsy, however, PBB suffers from two disadvantages: firstly it can only provide information on transmission through the maternal line, and secondly it involves gre-

ater uncertainty since the results of testing cannot be checked using a second cell. The advantage of PBB lies in the fact that it does not give rise to an embryo that would then have to be discarded. At present, despite the ban on PGD, PBB is legal in Switzerland and is actually offered at a few centres. If, because of a ban on PGD, PBB is the only legal way of averting the risk of disease, then a gender issue arises, since diseases transmitted by the woman can be diagnosed prior to pregnancy while those passed down by the man cannot be detected at that stage.

The ethical concerns expressed about PBB are limited to the fact that the procedure requires a fairly large number of inseminated oocytes, the procurement of which may possibly involve an increased risk for the woman concerned. However, there is a good case for arguing that the assessment of these risks should be a matter for the woman herself. The state should not paternalistically disregard her wishes. PBB is, however, rightly preferred for medical reasons in cases where a disease can only be transmitted maternally (e.g. Duchenne muscular dystrophy). The risk to the child is then lower with PBB than with PGD.

3.8 Demarcation issues

One of the key questions is whether, if limits are not to be defined via a positive/negative list, this should be done instead through general formulations such as «serious disease», «serious untreatable disease», «serious familial disease», «disease leading to death in the first year of life» or a similar expression. In everyday life, people have a certain conception of a «serious disease». However, the expression is vague, and grey areas exist. Even chromosomal anomalies cannot always be unequivocally described as «serious diseases», as in the case of trisomy 21, for example. What is to be termed a «serious disease» depends on value judgments. Various questions and aspects have been raised:

- Could efforts to detect mutations that involve a risk of disease (e.g. breast or bowel cancer) be excluded?
- There must be no obligation to perform diagnosis or to discard an embryo in the event of abnormalities being found. This must be excluded by the law. The formula used to define limits for the application of PGD should not serve as a eugenic criterion.
- A list of diseases is not to be recommended since (1) borderlines will be drawn on an individual basis, (2) the severity of expression may be influenced by epigenetic factors and (3) such a list would have discriminatory effects.
- Borderlines can only be drawn by the parents. But how are they to know in advance how bad a given genetically detectable disease is?
- An argument against taking the treatability of a disease as a contraindication to PGD is the fact that this would also exclude, for example, haemophilia; while this condition is treatable, its management and the prevention of consequences impose major burdens and restrictions on those concerned. Any restriction of PGD to diseases that are fatal in the first year of life or to familial disorders will inevitably appear to be arbitrary and is therefore scarcely to be recommended.
- Among those who may transmit a genetic disease, a distinction is drawn between the indications of adversity and risk. For example, advanced reproductive age represents a risk-based indication in women undergoing IVF. IVF with PGD will therefore probably also be desired by some non-infertile subjects in order to reduce this risk. To define the risk of the occurrence of a serious disease, a general formulation such as «substantial risk» would also have to be used.
- Also to be considered are cases where carrier status for a recessive disorder is to be deter-

mined, or a disease that may occur later in life. An example of the former would be cystic fibrosis, which is only expressed in the event of mutations in both alleles. An example of the latter would be Huntington's disease, which only manifests itself in the patient's fourth or fifth decade. While carrier status has no adverse effects on the health of the child concerned, the transmission of a fatal late-onset disease can have dramatic consequences for those concerned. It would be arbitrary to accord lesser importance to a disease occurring in middle age than to an early-onset disease.

Chapter IV: Recommendations of the NEK-CNE

Within the Commission, there are two opposing views as to how PGD should be legally regulated. One position, calling for the complete ban to be maintained, is adopted by a minority of Commission members. The second position supports a relaxation of the ban, with the introduction of more nuanced regulations that would restrict PGD to certain indications. This is advocated by the majority of Commission members.

Minority position: PGD should remain prohibited.

Statement of reasons:

- The act of PGD differs qualitatively from that of PD. In one case, a woman has to decide whether to continue with or to terminate an existing pregnancy. In the other case, one embryo is chosen from several that have been created for the purposes of selection.
- Selection of human life is contrary to human dignity, which essentially requires that people should never be treated merely as means but always also as ends in themselves. Although the members of this minority within the Commission do not assume that the early embryo can be a person in the sense of a subject of fundamental constitutional rights (to life, physical integrity, etc.), they still maintain that the instrumentalization of human embryos is ethically reprehensible.
- PGD promotes the illusion of safety in the sense of avoidability of disease and disability. At the same time, there is no guarantee that in society and in families PGD, together with PD, will not also lead to discrimination against children with disabilities.
- It will scarcely be possible to provide a clear-cut definition of the notion of «serious disease». It could soon shift away from the most severe genetic defects towards remediable disabilities or even further, towards aesthetically displeasing physical characteristics.
- There is also a risk that the PGD method will give rise to further methods for the production of artificial embryos which are not foreseeable at present.

Majority position: The ban on PGD should be lifted and be replaced by nuanced regulations restricting the provision of PGD to certain indications and prohibiting its application outside these indications. The indications should be confined, in a restrictive manner, to avoidance of the risk of serious diseases or disabilities for the person concerned.

PGD should be permitted in the following situations:

1. If there is a risk of a serious disease that can already be diagnosed in an embryonic cell.
2. For couples undergoing an IVF procedure for the treatment of infertility.

PGD should be prohibited in all other situations, in particular:

1. Selection for the benefit of a third party, i.e. in order to create a child that could donate cells, tissue or organs to someone suffering from a disease.
2. Exclusion of carrier status for a recessively inherited disease.
3. Selection of non-disease-related characteristics, including the child's sex – except in cases where a disease is sex-linked.

Appropriate measures, based on the requirements concerning PD in the Federal Act on Genetic Testing of Human Beings (GUMG), are to be taken to ensure that PGD, newly introduced in Switzerland, is accompanied by adequate **provision of counselling**, covering medical, genetic, ethical and psychosocial aspects. Counselling is to be initiated prior to any decision to carry out PGD. It should be designed to counteract any kind of pressure affecting the autonomy of the couple and especially the woman, and to support considered and informed decision-making, also giving due consideration to alternative options. The Commission is concerned to ensure that, when couples decide whether a reproductive medical measure is to be carried out, they are openly informed about the associated risks and burdens for the woman and especially also for the child. It should be clearly pointed out to the couples concerned that there can be no guarantee of a healthy child even if PGD is performed.

In parallel, PGD should be **scientifically evaluated**. In addition to long-term medical consequences, this evaluation should investigate social and psychological effects. If appropriate, the results of these studies should be systematically incorporated into a revision of the regulations proposed here.

For purposes of legislation, a question that needs to be clarified is how the term **«serious disease»** is to be operationally defined. A lack of effective treatments is not to be adopted as a general requirement. The relevant issues are to be weighed up on an individual basis, in full knowledge of the circumstances and implications of the treatments in question. Estimating how high the identifiable risk of a disease needs to be for PGD to be indicated should be a matter for individual assessment in the context of genetic counselling. In accordance with the Federal Constitution and the Reproductive Medicine Act (FmedG), non-infertile couples should also have access to medically assisted reproductive techniques in the event of a risk of serious disease.

Polar body biopsy should remain permissible, but like PD it should only be performed in cases where it is justified on preventive medical grounds, and counselling is to be provided before and after the test. In this counselling, reference should be made to the limited scope and reliability of polar body testing.

The question of whether and in what circumstances **research** may be carried out on embryos that are diagnosed as affected by disease and that cannot be transferred is subject to the provisions of the Stem Cell Research Act and is also to be regulated in the Human Research Act.

Statement of reasons:

- Of central concern are those couples whose children are exposed to a substantial risk of suffering from a serious genetic disease. Under current Swiss legislation, the only option available for couples who do not wish to transmit the disease to their children is to embark on a pregnancy and, if PD shows the fetus to be affected, consider a termination. In such cases, PGD could represent a useful alternative. On ethical grounds, prohibition of this method is unacceptable for the couples and particularly the women concerned. Provided that this method is available and sufficiently safe, it spares them the need to embark on a «trial» pregnancy. However, this justification applies only to couples who know that the fetus or child faces a risk of serious disease.
- PGD restricted to these indications helps to avoid terminations carried out on account of fetal disease. From the perspective of protection of developing human life, non-transfer of an early embryo at the blastocyst stage is less serious than the killing of a fetus at a more advanced stage of development in the course of pregnancy.
- The various objections raised and the reasons that led to the prohibition of PGD in Switzerland can be addressed by the adoption of the restrictive indication-based regulatory ap-

proach.

- Decisive efforts are to be made to prevent any loss of solidarity with the sick and disabled. However, the ban on PGD is not a suitable measure for this purpose.
- It would not be advisable to restrict PGD in the context of IVF treatment to cases where there is an increased risk of chromosomal anomalies on account of the woman's age or similar factors. This would amount to discrimination against women who do not fulfil any of the recognized criteria for «increased risk».
- It is recommended that limits should be defined on the basis of the concept of «serious disease», rather than by drawing up a positive/negative list of diseases that are to be included/excluded. Such a list is not advisable for three reasons: (1) even with the same genetics and the same physical manifestations, the seriousness of a disease also depends on the burden of suffering as perceived by the individual patient; (2) the severity of phenotypic expression is also influenced by epigenetic factors; and (3) a list could have discriminatory effects both for people with a listed disease and for those not included in such a list.
- Situations in which PGD is indicated need to be distinguished from situations in which the child faces no risk of serious disease or disability. Otherwise the use of PGD would become a eugenic measure rather than one designed to prevent disease.