Catholic On Call handbook
Chapter 5 - Genetic testing and research

The Catholic MO/HO: Medical research may benefit man but must always be conducted in such a manner that upholds the dignity of the human person and with the subjects'consent. Prenatal diagnosis may be morally licit if it respects the life and integrity of the embryo and is directed toward its safeguarding or healing as an individual.

5.1 Basic Church teaching

5.1.1 Catechism of the Catholic Church (CCC)

" Basic scientific research, as well as applied research, is a significant expression of mans dominion over creation. Science and technology are precious resources when placed at the service of man and promote his integral development for the benefit of all. By themselves, however they cannot disclose the meaning of existence and of human progress." (CCC, 2293)

"It is an illusion to claim moral neutrality in scientific research and its applications….Science and technology by their very nature require unconditional respect for fundamental moral criteria. They must be at the service of the human person…" (CCC, 2294)

"Research or experimentation on the human being cannot legitimate acts that are in themselves contrary to the dignity of persons and to the moral law. The subjects' potential consent does not justify such acts. Experimentation on human beings is not morally legitimate if it exposes the subject's life or physical and psychological integrity to disproportionate or avoidable risks. Experimentation on human beings does not conform to the dignity of the person if it takes place without the informed consent of the subject or those who legitimately speak for him." (CCC,2295)

"Since it must be treated from conception as a person, the embryo must be defended in its integrity, cared for, and healed, as far as possible, like any other human being.

Prenatal diagnosis is morally licit, "if it respects the life and integrity of the embryo and the human fetus and is directed toward its safeguarding or healing as an individual….It is gravely opposed to the moral law when this is done with the thought of possibly inducing an abortion, depending upon the results: a diagnosis must not be the equivalent of a death sentence." (CCC, 2274)

"One must hold as licit procedures carried out on the human embryo which respect the life and integrity of the embryo and do not involve disproportionate risks for it, but are directed toward its healing, the improvement of its condition of health, or its individual survival.

It is immoral to produce human embryos intended for exploitation as disposable biological material.

Certain attempts to influence chromosomal or genetic inheritance are not therapeutic but are aimed at producing human beings selected according to sex or other predetermined qualities. Such manipulations are contrary to the personal dignity of the human being and his integrity and identity which are unique and irreplaceable." (CCC, 2275)

5.1.2 Excerpts from ***Instruction on Respect for Human Life in its Origin and on the Dignity of Procreation or Donum Vitae*** (Prepared by the Sacred Congregation for the Doctrine of the Faith, February 22, 1987, the feast of St Peter):

"The moral relevance of the link between the meanings of the conjugal act and between the goods of marriage, as well as the unity of the human being and the dignity of his origin, demand that the procreation of a human person be brought about as the fruit of the conjugal act specific

to the love between spouses."

"....the child must be respected and recognized as equal in personal dignity to those who give him life."

"The child is not an object to which one has a right, nor can he be considered as an object of ownership...."

"....subjectively good intentions do not render heterologous artificial fertilization conformable to the objective and inalienable properties of marriage or respectful of the rights of the child and of the spouses."

"If the technical means facilitates the conjugal act or helps it to reach its natural objectives, it can be morally acceptable. If, on the other hand, the procedure were to replace the conjugal act, it is morally illicit."

"The process of in vitro fertilisation (IVF) and embryo transfer (ET) must be judged in itself and cannot borrow its definite moral quality from the totality of conjugal life of which it becomes part nor from the conjugal acts which may precede or follow it."

"....the so-called 'simple case' i.e. a homologous IVF and ET procedure that is free of any compromise with the abortive practice of destroying embryos and with masturbation, remains a technique which is morally illicit because it deprives human procreation of the dignity which is proper and connatural to it."

"No objective, even though noble in itself, such as a foreseeable advantage to science, to other human beings or to society, can in any way justify experimentation on living human embryos or foetuses, whether viable or not, either inside or outside the mother's womb. The informed consent ordinarily required for clinical experimentation on adults cannot be granted by the parents, who may not freely dispose of the physical integrity or life of the unborn child."

5.1.3 *Excerpts from* ***Declaration on the production and the scientific and therapeutic use of human embryonic stem cells*** *(*Prepared by the Pontifical Academy for Life, Vatican City, August 25, 2000)

1. ***Is it morally licit to produce and/or use living human embryos for the preparation of embryonic stem cells?*** *The answer is negative. On the basis of a complete biological analysis, the living human embryo is - from the moment of the union of the gametes - a human subject with a well defined identity, which from that point begins its own coordinated, continuous and gradual development, such that at no later stage can it be considered as a simple mass of cells.*
2. ***Is it morally licit to engage in so-called "therapeutic cloning" by producing cloned human embryos and then destroying them in order to produce ES cells?*** *The answer is negative, for the following reason: Every type of therapeutic cloning, which implies producing human embryos and then destroying them in order to obtain stem cells, is illicit.*
3. ***Is it morally licit to use embryonic stem cells, and the differentiated cells obtained from them, which are supplied by other researchers or are commercially obtainable?*** *The answer is negative, since prescinding from the participation - formal or otherwise - in the morally illicit intention of the principal agent, the case in question entails a proximate material cooperation in the production and manipulation of human embryos on the part of those producing or supplying them.*

5.1.5 Excerpts from **Dangers of Genetic Manipulation** (Address by Pope John Paul II to members of the World Medical Association (October 29, 1983)

"Genetic manipulation becomes arbitrary and unjust when it reduces life to an object, when it forgets that it is dealing with a human subject, capable of intelligence and freedom, worthy of respect whatever may be their limitations; or when it treats this person in terms of criteria not founded on the integral reality of the human person, at the risk of infringing upon his dignity. In this case, it exposes the individual to the caprice of others, thus depriving him of his autonomy."

"....speak of 'genetic surgery' so as to show more clearly that medicine intervenes not in order to modify nature but to favour its development in its own life, that of the creation, as intended by God."

"Moreover, the fundamental attitudes that inspire the interventions of which we are speaking should not flow from a racist and materialist mentality aimed at a human well-being that is, in reality, reductionist. The dignity of man transcends his biological condition."

5.2 Issues in clinical practice

5.2.1 Definitions and basic information

Genetic testing – the analysis of human DNA, RNA, genes and/or chromosomes, or the analysis of human proteins or certain metabolites, with the primary purpose of detecting a heritable genotype, mutation, phenotype or karyotype.

Genetic testing may be done for research or clinical purposes.

Clinical genetic testing subsumes the following:

(a) Confirmatory diagnosis for specific genetic disorders
(b) Carrier testing for recessive disorders
(c) Pre-implantation genetic testing (PIGD) on embryos created by *in vitro* fertilisation, for the purpose of selecting or excluding embryos for implantation into the uterus (including sex selection). May be used with pre-implantation tissue typing to select immunogenetically compatible child as potential stem cell donor to a sick sibling.
(d) Prenatal genetic testing (PNGD) to identify a specific genetic disorder in a foetus
(e) Predictive testing of asymptomatic individuals to identify genes for late-onset disease that normally becomes symptomatic only in adulthood
(f) Genetic screening of healthy individuals at increased risk for developing a particular genetic condition. Aims to prevent disease or minimise morbidity/mortality through early diagnosis and treatment.

Prenatal genetic testing and diagnosis of the embryo or foetus is licit only if it is directed toward its safeguarding or healing as an individual. It is immoral to counsel, establish, collaborate with or otherwise link any such procedure to an abortion or to use or request it as a search and destroy tool against unborn babies with developmental imperfections. Genetic counselling targeted at abortion is formal co-operation and therefore illicit.

Ultrasound and Amniocentesis (the latter commonly done at 15-18 weeks for the purpose of abortion) may nevertheless be licit and useful in the third trimester, since abortion is illegal after 24 weeks. Similarly, therapeutic procedures such as some corrections of chromosomal defects can be licit if directed towards healing and if there are no disproportionate risks. This excludes manipulation for eugenic or commercial reasons.

Procurement of genetic material for prenatal testing:

(a) Amniocentesis
- outpatient procedure in which the obstetrician withdraws a small amount of amniotic fluid (20 ml) surrounding the foetus using thin hollow needle inserted into the mother's abdomen under ultrasound guidance
- performed between the 16th and 20th weeks of pregnancy
- analysis of foetal cells in amniotic fluid to detect chromosomal abnormalities such as trisomy 21 (Down syndrome)
- results take 3-4 weeks
- risk of miscarriage reported to be 0.3-0.5% following the test

(b) Chorionic villus sampling
- outpatient procedure in which the obstetrician withdraws a small amount of placental tissue by inserting a biopsy needle through the mother's abdomen under ultrasound guidance. Local anaesthesia is used.
- performed between the 10th and 12th weeks of pregnancy
- able to detect chromosomal disorders and genetic diseases such as thalassaemia
- results take 3-4 weeks
- risk of miscarriage reported to be 1% following the test

(c) Foetal blood sampling
- outpatient procedure in which the obstetrician withdraws blood from the umbilical cord of the foetus using a thin hollow needle inserted through the mother's abdomen into the umbilical cord under ultrasound guidance
- performed between the 20th and 23rd week of pregnancy
- detects chromosomal disorders, genetic disorders and viral infection
- results take 1-2 weeks
- risk of miscarriage reported to be 2-5% following the procedure

Other prenatal tests include maternal serum screening and first trimester screening.

(a) Maternal serum screening (MSS)
- blood test conducted between 15th and 20th week of pregnancy to aid in risk assessment of trisomy 21 (Down syndrome)
- results usually available within 3 days
- measures serum levels of alphafetoprotein (AFP) and hCG (human chorionic gonadotrophin) in maternal blood*
- calculation using maternal age, AFP and hCG levels performed to determine individual maternal risk of having a child with Down syndrome. Classified into "low-risk" or "high-risk" categories with cut-off risk of 1 in 250. Mothers in "high-risk" category are offered amniocentesis.
- May also detect spina bifida**
- 6-7 out of 10 babies with Down syndrome will be detected using MSS. However, a "high-risk" result does not mean that the baby has Down syndrome. Likewise, a "low-risk" result does not mean that the baby is healthy.
- Rate of detection for mothers at "high risk" varies according to maternal age

Maternal age	Detection rate
Less than 20 years	46 %
Between 20 - 24 years	47 %
Between 25 - 29 years	50 %
Between 30 - 34 years	60 %
Between 35 - 39 years	77 %
Over 40 years	91 %

* Low AFP and high hCG are suggestive of Down syndrome
** High AFP is suggestive of spina bifida

(b) First trimester screening for Down syndrome
- OSCAR: one-stop clinic for assessment of risk for foetal anomalies
- Introduced by Fetal Medicine Foundation (United Kingdom)
- For detection of Down syndrome in first trimester
- Performed between the 11th and 13th week of pregnancy
- Reported detection rate of 90%
- Includes measurement of serum levels of PAPP-A (pregnancy-associated plasma protein A) and free β-hCG, as well as ultrasound measurement of nuchal translucency
- Computer software used to calculate risk of Down syndrome, trisomies 13 and 18 in current pregnancy
- Test regarded as positive if computed chance higher than 1:180 for Down syndrome and 1:150 for trisomies 13 and 18
- Further invasive procedures (chorionic villus sampling or amniocentesis) required for confirmation

Genetic counselling – provision of sufficient and unbiased information regarding genetic conditions/diseases, genetic testing and interpretation of test results to enable full and informed choices to be exercised, as well as appropriate support to patient and family members

Gene therapy - the deliberate alteration of the genetic material of living cells to prevent or treat disease.

5.2.2 Medical experimentation (interventional) and Research (inductive-deductive processes)

Medical Research and Experimentation that is not **directly** therapeutic on a live embryo or foetus, is immoral from the moment of conception irrespective of how the embryo was formed e.g. spare embryos from IVF. This includes any research on human embryonic pluripotent stem cells that separates the inner cell mass and kills or harms the embryo, as well as the therapeutic use of the products of such research, even if of medical benefit to others. Every person must be respected for himself. There is also an injunction against fusion of human and animal gametes, gestation of humans in animal, artificial or surrogate uteri and all methods for obtaining human beings without sexuality such as by "twin fission" of an embryo, cloning or parthenogenesis.

But as much as IVF is wrong, embryos from IVF or cloning must not be experimented upon, destroyed or cryopreserved even to save life as in embryo banks, or subjected to commercialism. Trafficking in or improper disposal of the dead body of an embryo or foetus is also wrong. All these assaults are contrary to the personal dignity of the embryo as a human being and his or her integrity and identity, and his right to be conceived and born within marriage and from marriage.

Human Cloning ("in-vitro fusion") is always wrong for the same reasons as IVF ("in-vitro fertilisation"). Cloning or somatic cell nuclear transfer combines an enucleated ovum of a mammal with an adult human nucleus or cell that has undergone some process to regain totipotent capacity. For example, cow ova will sustain other mammalian nuclei. Electrical stimuli are used to fuse them and so obtain embryonic pluripotent stem cells and organs (**"therapeutic cloning"**) or, with the further addition of a trophoblast cell to grow a placenta, adult clones of the animal that donated the nucleus (**"reproductive cloning"**). Transfer of human genes to an animal (**transgenic animal**), with or without subsequent cloning of the animal, needs further

study. At stake perhaps is the amount of "humanness" that can be licitly transferred to an animal such as a cow to make it produce human milk or to a chimpanzee to make it more intelligent. Tissue culture of specialised cell lines (skin, marrow, bones) may be licit if not derived through any illicit procedures.

5.2.3 Genetic manipulation (surgery)

Genetic manipulation or rather genetic surgery in a human being may be licit if it is used not to modify nature but to favour its development as intended by God, by correcting anomalies such as certain hereditary illnesses. It would naturally be illicit if these manipulations were carried out as an extension of an illicit procedure such as IVF or human cloning, to modify genetic inheritance or to create marginalized groups in society. Further information is needed in the case of transfer of genetic material between humans and animals (transgenic animals) and between humans. Such gene transfers might be used as gene therapy or to produce animal organs compatible with human immunological defences.

5.2.4 Legal issues

5.2.4.1 Medical (Therapy, Education and Research) Act (MTERA)

(Chapter 175) (Original Enactment: Act 23 of 1972)
Revised edition 1985 (30th March 1987)
An Act to make provision for the use of the bodies of deceased persons or parts thereof for purposes of medical or dental education, research, advancement of medical or dental science, therapy and transplantation, and for other purposes connected therewith. [25th May 1973]

Comparison of organ donation under the HOTA and MTERA in Singapore

	HOTA	**MTERA**
Age	21 years old and above	Age limit for organ pledging: 18 years and above The adult next-of-kin can also pledge the organs of deceased patients of any age for donation.
Organs included	Kidney Liver Heart Cornea	All organs and tissues e.g. kidney, liver, heart, cornea, lung, bone, skin
Purpose(s)	Transplant	Transplant and treatment Education Research
Nationality	Singapore citizens and PRs	Any nationality
Religion	Any religion (Muslims were included under HOTA from 1 August 2008)	Any religion (For Muslims, MUIS has issued fatwas stating that the donation of kidney, liver, heart and cornea is permissible.)
Consent	Opt-out *People who meet the above criteria will be automatically included under HOTA unless they register their objection.*	Opt-in *People who are not covered under HOTA, as well as people who wish to pledge any organ/tissue not covered by HOTA, will only have their organs removed if they have pledged their organs/tissues for donation.*

5.2.4.2 Human Cloning and Other Prohibited Practices Act
This Act was passed by Parliament in September 2004 and came into effect on 1 October 2004.

The Act has the following provisions:

1. **To prohibit the implantation of any human clone into the body of a woman**
   This effectively prevents a human clone from being implanted into a human womb for gestation to full term.
2. **To prohibit against developing embryos outside the human body for more than 14 days**
   This would address any attempt to circumvent the first provision by developing the embryo into a viable foetus outside of a human body. The cut-off point of 14 days was used as the cells start to differentiate and form tissues around that period. This 14-day rule is found in similar legislation in countries such as Australia, Belgium, Japan and the UK.
3. **To prohibit against certain uses of embryos** to prevent repugnant experimentation such as placing a human embryo in an animal or placing an animal embryo into a human.
4. **To prohibit the implantation of "prohibited embryos"** such as embryos which have been developed outside of a woman's body for more than 14 days.
   The Act also bans the deliberate removal of an embryo from a woman's body with the intention of obtaining a viable embryo.
5. **To prohibit against import and export of prohibited embryos**
   This ensures that local scientists do not collaborate with overseas parties in unethical human cloning research activities.
6. **Prohibition of commercial trading in egg, sperm and embryo**.
   This prevents the giving of valuable consideration such as money or gifts in exchange for a supply of egg, sperm or embryo, but does not refer to the reasonable reimbursement of expenses incurred or services provided in the collection, storage of transport of the tissue.
7. **Penalties**
   The maximum penalties for offences under this Act are a $100,000 fine, a 10 year jail term, or both.

5.2.4.3 Report of the Bioethics Advisory Committee, Singapore on genetic testing and genetic research

About the Bioethics Advisory Committee
The Bioethics Advisory Committee (BAC) was established by the Singapore Cabinet in December 2000. The BAC was directed to "examine the legal, ethical and social issues arising from research on human biology and behaviour and its applications" and to "develop and recommend policies on legal, ethical and social issues, with the aim to protect the rights and welfare of individuals, while allowing the Life Sciences to develop and realise their full potential for the benefit of mankind."
The BAC reports to the Life Sciences Steering Committee (formerly Life Sciences Ministerial Committee).
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The most distinctive feature of genetic information is its predictive power for individuals and their close relatives. Informed consent for testing with pre-and post-test counselling is required. Care with interpretation is advisable as it is generally probabilistic in nature.

Vulnerable persons such as children and adolescents, the mentally impaired and other persons in dependent relationships (e.g. prisoners, students) require special safeguards.

(a) Children and adolescents
- May be regarded as mature enough to consent for genetic testing if capable of understanding the purpose and implications of test
- Carrier testing should generally be deferred till child is sufficiently mature or has to make reproductive decisions. Exceptions may exist in certain cases where family members may benefit (e.g. identify need for further screening in relatives) or public health imperatives exist (e.g. eradication of certain diseases)
- Predictive testing in children is not encouraged unless there are preventive measures available in childhood

(b) Mentally impaired individuals
- Important consideration is whether genetic testing is in the individual's best interest
- Exceptions may exist where an imperative need exists for the confirmatory diagnosis of genetic disease in related family members where it would change medical management

(c) Persons in dependent relationships
- Important to ensure that consent is truly voluntary and that no benefits currently provided or in prospect would be jeopardised by a refusal

Genetic testing should be done by qualified healthcare professionals and availability of tests providing predictive health information directly to the public without appropriate and timely medical consultation should be limited, owing to the potential risks of misinformation and risk of testing without consent.

5.2.5 Suggested approaches to common clinical scenarios

1. **Prenatal genetic testing**

a. **Pregnant woman asking for prenatal genetic diagnosis of thalassaemia in baby as both she and her husband are thalassaemia minor carriers**

- Pray for the Lord's guidance before beginning the consult.
- Take a basic history: current gestation, maternal iron/folate supplementation (if any), exact genetic diagnosis of both parents (if genetic analysis for thalassaemia previously performed)
- Explore ***reasons/s for wanting prenatal diagnosis***
- Explain procedure of prenatal testing (chorionic villus sampling) and that the test is not 100% accurate
- Mention current treatment advances in thalassaemia, including possibility of cure by bone marrow transplant
- Offer a follow-up visit to discuss patient's concerns further if indicated
- Say a prayer for your patient and her husband/family

2. **Parents asking for genetic testing for young child for heritable adult-onset disease in family (BRCA gene for breast/ovarian malignancies, Huntington disease)**

- Pray for the Lord's guidance before beginning the consult.
- Take a basic history: family tree of affected relatives for disease in question (note type of genetic inheritance), parents'/child's personal knowledge/experience of and beliefs regarding said disease, available treatment and prognosis, current

understanding regarding genetic test/s recommended/sought including test accuracy/concepts of inheritance *vs*. penetrance (i.e. positive test does not equate clinical manifestation of disease)
- Gently counsel that ***test should not be performed unless therapeutic/preventive measures available in childhood***
- Raise awareness of potential harm to child of genetic testing before child is mature enough to give informed consent/make own medical/reproductive decisions (e.g. psychological distress, adoption of sick role, making erroneous decisions about marriage and child-bearing based on incomplete understanding of said disease, insurance coverage etc.)
- ?offer referral to (Catholic) geneticist or genetic counsellor to clarify doubts/further questions
- Offer follow-up visit to discuss parents'/child's concerns

3. **Medical student doing laboratory research seeking advice regarding therapeutic/reproductive cloning in the lab**

- Pray for the Lord's guidance before beginning the consult.
- Ask about proximity of involvement of student in said research (i.e. direct involvement in cloning process *vs.* use of cloned cells in research *vs.* working on separate research project/s in lab where cloning is performed)
- Explain that ***human cloning is immoral and therefore always wrong***
- Refer student to CMG spiritual director or other moral theologians for discussion of specific situations/to clarify further questions and doubts

4. **Clinician-scientist seeking advice regarding the use of gene therapy to treat enzyme deficiencies in patients with rare metabolic diseases**

- Pray for the Lord's guidance before beginning the consult.
- Explore nature of clinician-scientist's involvement in gene therapy: usage *vs.* research into *vs.* creation of therapeutic gene product, alternative therapies available (e.g. enzyme replacement)
- Explain that ***gene therapy may be licit if it is used not to modify nature but to favour its development as intended by God***, by correcting anomalies such as certain hereditary illnesses (as in this case)
- Need to explore how therapeutic gene/vector is derived
- Refer student to CMG spiritual director or other moral theologians for discussion of specific situations/to clarify further questions and doubts

5.3 References

1. Evangelium Vitae
2. Donum Vitae
3. Dignitatis Personae
4. **Declaration on the production and the scientific and therapeutic use of human embryonic stem cells** *(*Prepared by the Pontifical Academy for Life, Vatican City, August 25, 2000)
5. **Dangers of Genetic Manipulation** (Address by Pope John Paul II to members of the World Medical Association (October 29, 1983)
6. **Report of the Bioethics Bioethics Advisory Committee, Singapore on genetic testing and genetic research** (Nov 2005)