

The International Committee for Monitoring Assisted Reproductive Technology (ICMART) and the World Health Organization (WHO) Revised Glossary on ART Terminology, 2009[†]

F. Zegers-Hochschild^{1,9}, G.D. Adamson², J. de Mouzon³, O. Ishihara⁴, R. Mansour⁵, K. Nygren⁶, E. Sullivan⁷, and S. van der Poel⁸ on behalf of ICMART and WHO

¹Unit of Reproductive Medicine, Clinicas las Condes, Santiago, Chile ²Fertility Physicians of Northern California, Palo Alto and San Jose, California, USA ³INSERM U822, Hôpital de Bicêtre, Le Kremlin Bicêtre Cedex, Paris, France ⁴Saitama Medical University Hospital, Moroyama, Saitama 350-0495, JAPAN ⁵3 Rd 161 Maadi, Cairo 11431, Egypt ⁶IVF Unit, Sophiahemmet Hospital, Stockholm, Sweden ⁷Perinatal and Reproductive Epidemiology and Research Unit, School Women's and Children's Health, University of New South Wales, Sydney, Australia ⁸Department of Reproductive Health and Research, and the Special Program of Research, Development and Research Training in Human Reproduction, World Health Organization, Geneva, Switzerland

⁹Correspondence address: Unit of Reproductive Medicine, Clinica las Condes, Lo Fontecilla, 441, Santiago, Chile. Fax: 56-2-6108167, E-mail: fzeegers@clc.cl

BACKGROUND: Many definitions used in medically assisted reproduction (MAR) vary in different settings, making it difficult to standardize and compare procedures in different countries and regions. With the expansion of infertility interventions worldwide, including lower resource settings, the importance and value of a common nomenclature is critical. The objective is to develop an internationally accepted and continually updated set of definitions, which would be utilized to standardize and harmonize international data collection, and to assist in monitoring the availability, efficacy, and safety of assisted reproductive technology (ART) being practiced worldwide.

METHOD: Seventy-two clinicians, basic scientists, epidemiologists and social scientists gathered together at the WHO headquarters in Geneva, Switzerland in December, 2008. Several months in advance, three working groups were established which were responsible for terminology in three specific areas: clinical conditions and procedures, laboratory procedures and outcome measures. Each group reviewed the existing ICMART glossary, made recommendations for revisions and introduced new terms to be considered for glossary expansion.

RESULTS: A consensus was reached on 87 terms, expanding the original glossary by 34 terms, which included definitions for numerous clinical and laboratory procedures. Special emphasis was placed in describing outcome measures such as cumulative delivery rates and other markers of safety and efficacy in ART.

CONCLUSIONS: Standardized terminology should assist in analysis of worldwide trends in MAR interventions and in the comparison of ART outcomes across countries and regions. This glossary will contribute to a more standardized communication among professionals responsible for ART practice, as well as those responsible for national, regional and international registries.

Introduction

The need for standard definitions is critical for benchmarking the outcomes of assisted reproductive technology (ART) procedures, at both a national and international level. Increase in the use of ART treatment worldwide and the continuing discussions, controversies and debates

over measures of efficacy and safety have generated both scientific and public interest (GD Adamson et al, 2006; J de Mouzon et al, 2004; RP Dickey, 2007; European IVF Monitoring Consortium Report, ESHRE, 2008). Definitions used in medically assisted reproduction within different countries are frequently the result of adaptations to particular medical, cultural and religious settings. However, when undertaking

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international data collection, standardization is necessary so that monitoring of efficacy, safety and quality of procedures and multinational research can be undertaken.

The International Committee for Monitoring Assisted Reproductive Technology (ICMART), an entity responsible for the collection and dissemination of worldwide data on ART, published the first glossary on ART terminology in 2006 (Zegers-Hochschild, 2006, *Fertil Steril*; Zegers-Hochschild, 2006, *Hum Reprod*). That particular glossary resulted from discussions by participants at an international meeting on "Medical, Ethical and Social Aspects of Assisted Reproduction" organized by the WHO in 2001 (ICMART, The ICMART glossary, Report of a WHO meeting, 2002).

In December 2008, the WHO with the assistance of the ICMART, the Low Cost IVF Foundation (LCIVFF) and the International Federation of Fertility Societies (IFFS), organized an international WHO meeting on "Assisted Reproductive Technologies: Common Terminology and Management in Low-Resource Settings". ICMART members and the WHO were responsible for steering an extensive review and improvement of the already existing "Glossary on ART Terminology" (Zegers-Hochschild, 2006, *Fertil Steril*; Zegers-Hochschild, 2006, *Hum Reprod*). They were guided by the objective of developing an internationally accepted set of definitions that would help standardize and harmonize international data collection to monitor the availability, efficacy, and safety of ART interventions to achieve high quality data in all settings including low-resource settings.

The WHO, in collaboration with the organizing committee, gathered health professionals from developed and developing countries, who were selected for their expertise and/or as representatives of major international and national reproductive health medical organizations, including the American Society for Reproductive Medicine (ASRM), the European Society for Human Reproduction and Embryology (ESHRE), the International Committee for Monitoring Assisted Reproductive Technology (ICMART), the Red Latino Americana de Reproducción Asistida (RED), the International Federation of Fertility Societies (IFFS), the International Federation of Gynaecology and Obstetrics (FIGO), the Middle East Fertility Society (MEFS), the Japan Society for Reproductive Medicine (JSRM), the Japan Society for Obstetrics and Gynaecology (JSOG), the Society of Obstetrics and Gynaecology of Burkina (SOGOB), the Chinese Society of Reproductive Medicine, the Indian Society for Assisted Reproduction, the Brazilian Society of Assisted Reproduction (SBRA), the World Endometriosis Society (WES), the Fertility Society of Australia (FSA), the International Society for Mild Approaches to Assisted Reproduction (ISMAAR), the Russian Association of Human Reproduction (RAHR), the Asia Pacific Initiative on Reproduction (ASPIRE), and the Low Cost IVF Foundation (LCIVFF), as well as the editors of the journals *Fertility and Sterility* and *Human Reproduction*.

Working methodology

This revised and enhanced version of the ICMART glossary is the result of discussion and consensus reached among seventy-two (72) clinicians, basic scientists, epidemiologists and social scientists gathered together at the WHO headquarters in Geneva, Switzerland from December 1-5, 2008. Three working groups were established several months in advance. Each working group was responsible for reviewing the existing glossary and recommending new terminologies to represent clinical, laboratory and outcome measures.

The professionals facilitating each working group, in alphabetical order, were:

Clinical: David Adamson, Thomas D'Hooghe, Osamu Ishihara, Fernando Zegers-Hochschild.

Laboratory: Trevor Cooper, Outi Hovatta, Arne Sunde, Alan Trounson.

Outcome: Maryse Bonduelle, Jacques de Mouzon, Orvar Finnström, Hassan Sallam.

Each term, with its definition, was presented by the appropriate working group to all participants within sessions of the 2008 meeting at the WHO. The final version of this glossary was generated by meeting participants following thorough discussion, review of new and existing definitions, as well as opportunities throughout the week to engage the working groups for clarifications and suggestions before a final consensus on each term and definition was realized.

We anticipate this glossary will contribute to a more fluid communication among professionals responsible for ART practice, as well as those responsible for national, regional and international registries of ART data. Standardized terminology should assist analysis of worldwide trends and in the comparison of outcomes across countries and regions. This glossary does not include specific measures of "success" which would take into consideration the well-being of babies as well as of their mothers, fathers, surrogates and/or gamete donors.

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Glossary

Assisted hatching: an *in vitro* procedure in which the zona pellucida of an embryo is either thinned or perforated by chemical, mechanical or laser methods to assist separation of the blastocyst.

Assisted reproductive technology (ART): all treatments or procedures that include the *in vitro* handling of both human oocytes and sperm, or embryos, for the purpose of establishing a pregnancy. This includes, but is not limited to, *in vitro* fertilization and embryo transfer, gamete intrafallopian transfer, zygote intrafallopian transfer, tubal embryo transfer, gamete and embryo cryopreservation, oocyte and embryo donation, and gestational surrogacy. ART does not include assisted insemination (artificial insemination) using sperm from either a woman's partner or a sperm donor.

Biochemical pregnancy (preclinical spontaneous abortion/miscarriage): a pregnancy diagnosed only by the detection of HCG in serum or urine and that does not develop into a clinical pregnancy.

Blastocyst: an embryo, five or six days after fertilization, with an inner cell mass, outer layer of trophoblast and a fluid-filled blastocoel cavity.

Cancelled cycle: an ART cycle in which ovarian stimulation or monitoring has been carried out with the intention to treat, but did not proceed to follicular aspiration or, in the case of a thawed embryo, to embryo transfer.

Clinical pregnancy: a pregnancy diagnosed by ultrasonographic visualization of one or more gestational sacs or definitive clinical signs of pregnancy. It includes ectopic pregnancy. *Note: Multiple gestational sacs are counted as one clinical pregnancy.*

Clinical pregnancy rate: the number of clinical pregnancies expressed per 100 initiated cycles, aspiration cycles or embryo transfer cycles. *Note: When clinical pregnancy rates are given, the denominator (initiated, aspirated or embryo transfer cycles) must be specified.*

Clinical pregnancy with fetal heart beat: pregnancy diagnosed by ultrasonographic or clinical documentation of at least one fetus with heart beat. It includes ectopic pregnancy.

Congenital anomalies: all structural, functional, and genetic anomalies diagnosed in aborted fetuses, at birth or in the neonatal period.

Controlled ovarian stimulation (COS) for ART: pharmacological treatment in which women are stimulated to induce the development of multiple ovarian follicles to obtain multiple oocytes at follicular aspiration.

Controlled ovarian stimulation (COS) for non-ART cycles: pharmacological treatment for women in which the ovaries are stimulated to ovulate more than one oocyte.

Cryopreservation: the freezing or vitrification and storage of gametes, zygotes, embryos or gonadal tissue.

Cumulative delivery rate with at least one live born baby: the estimated number of deliveries with at least one live born baby resulting from one initiated or aspirated ART cycle including the cycle when fresh embryos are transferred, and subsequent frozen/thawed ART cycles. This rate is used when less than the

total number of embryos fresh and/or frozen/thawed have been utilized from one ART cycles. *Note: The delivery of a singleton, twin or other multiple pregnancy is registered as one delivery.*

Delivery: the expulsion or extraction of one or more fetuses from the mother after 20 completed weeks of gestational age.

Delivery rate after ART treatment per patient: the number of deliveries with at least one live born baby per patient following a specified number of ART treatments.

Delivery rate: the number of deliveries expressed per 100 initiated cycles, aspiration cycles or embryo transfer cycles. When delivery rates are given, the denominator (initiated, aspirated or embryo transfer cycles) must be specified. It includes deliveries that resulted in the birth of one or more live babies and/or stillborn babies. *Note: The delivery of a singleton, twin or other multiple pregnancy is registered as one delivery.*

Early neonatal death: death of a live born baby within 7 days of birth.

Ectopic pregnancy: a pregnancy in which implantation takes place outside the uterine cavity.

Elective embryo transfer: the transfer of one or more embryos, selected from a larger cohort of available embryos.

Embryo: the product of the division of the zygote to the end of the embryonic stage, eight weeks after fertilization. (This definition does not include either parthenotes - generated through parthenogenesis - nor products of somatic cell nuclear transfer.)

Embryo donation: the transfer of an embryo resulting from gametes (spermatozoa and oocytes) that did not originate from the recipient and her partner.

Embryo recipient cycle: an ART cycle in which a woman receives zygote(s) or embryo(s) from donor(s).

Embryo/fetus reduction: a procedure to reduce the number of viable embryos or fetuses in a multiple pregnancy.

Embryo transfer (ET): the procedure in which one or more embryos are placed in the uterus or Fallopian tube.

Embryo transfer cycle: an ART cycle in which one or more embryos are transferred into the uterus or Fallopian tube.

Extremely low birth weight: birth weight less than 1,000 grams.

Extremely preterm birth: a live birth or stillbirth that takes place after at least 20 but less than 28 completed weeks of gestational age.

Fertilization: the penetration of the ovum by the spermatozoon and combination of their genetic material resulting in the formation of a zygote.

Fetal death (stillbirth): death prior to the complete expulsion or extraction from its mother of a product of fertilization, at or after 20 completed weeks of gestational age. The death is indicated by the fact that, after such separation, the fetus does not breathe or show any other evidence of life such as heart beat, umbilical cord pulsation, or definite movement of voluntary muscles.

Fetus: the product of fertilization from completion of embryonic development, at eight completed weeks after fertilization, until abortion or birth.

Frozen/thawed embryo transfer cycle (FET): an ART procedure in which cycle monitoring is carried out with the intention of transferring a frozen/thawed embryo or frozen/thawed embryos. *Note: A FET cycle is initiated when specific medication is provided or cycle monitoring is started with the intention to treat.*

Frozen/thawed oocyte cycle: an ART procedure in which cycle monitoring is carried out with the intention of fertilizing thawed oocytes and performing embryo transfer.

Full-term birth: a live birth or stillbirth that takes place between 37 completed and 42 completed weeks of gestational age.

Gamete intrafallopian transfer (GIFT): an ART procedure in which both gametes (oocytes and spermatozoa) are transferred to the Fallopian tubes.

Gestational age: age of an embryo or fetus calculated by adding 2 weeks (14 days) to the number of completed weeks since fertilization. *Note: For frozen/thawed embryo transfers, an estimated date of fertilization is computed by subtracting the embryo age at freezing from the transfer date of the FET cycle.*

Gestational carrier (surrogate): a woman who carries a pregnancy with an agreement that she will give the offspring to the intended parent(s). Gametes can originate from the intended parent(s) and/or a third party (or parties).

Gestational sac: a fluid-filled structure associated with early pregnancy, which may be located inside or outside the uterus (in case of an ectopic pregnancy).

Hatching: the process by which an embryo at the blastocyst stage separates from the zona pellucida.

High-order multiple: a pregnancy or delivery with three or more fetuses or neonates.

Implantation: the attachment and subsequent penetration by the zona-free blastocyst (usually in the endometrium) that starts five to seven days after fertilization.

Implantation rate: the number of gestational sacs observed, divided by the number of embryos transferred.

In vitro fertilization (IVF): an ART procedure that involves extracorporeal fertilization.

Induced abortion: the termination of a clinical pregnancy, by deliberate interference that takes place before 20 completed weeks of gestational age (18 weeks post fertilization) or, if gestational age is unknown, of an embryo/fetus of less than 400 grams.

Infertility (clinical definition): a disease of the reproductive system defined by the failure to achieve a clinical pregnancy after 12 months or more of regular unprotected sexual intercourse.

Initiated cycle: an ART cycle in which the woman receives specific medication for ovarian stimulation, or monitoring in the case of natural cycles, with the intention to treat, irrespective of whether or not follicular aspiration is attempted.

IntraCyttoplasmic Sperm Injection (ICSI): a procedure in which a single spermatozoon is injected into the oocyte cytoplasm.

Live birth: the complete expulsion or extraction from its mother of a product of fertilization, irrespective of the duration of the pregnancy, which, after such separation, breathes or shows any other evidence of life such as heart beat, umbilical cord pulsation, or

definite movement of voluntary muscles, irrespective of whether the umbilical cord has been cut or the placenta is attached.

Live birth delivery rate: the number of deliveries that resulted in at least one live born baby expressed per 100 initiated cycles, aspiration cycles or embryo transfer cycles. When delivery rates are given, the denominator (initiated, aspirated, or embryo transfer cycles) must be specified.

Low birth weight: Birth weight less than 2,500 grams.

Medically Assisted Reproduction (MAR): reproduction brought about through ovulation induction, controlled ovarian stimulation, ovulation triggering, ART procedures, and intrauterine, intracervical, and intravaginal insemination with semen of husband/partner or donor.

MESA: Microsurgical Epididymal Sperm Aspiration.

MESE: Microsurgical Epididymal Sperm Extraction.

Micromanipulation: a technology that allows micro-operative procedures to be performed on the spermatozoon, oocyte, zygote or embryo.

MicroTESE: Microsurgical Testicular Sperm Extraction.

Mild ovarian stimulation for IVF: a procedure in which the ovaries are stimulated with either gonadotropins and/or other compounds, with the intent to limit the number of oocytes obtained for IVF to fewer than seven.

Missed abortion: a clinical abortion where the embryo(s) or fetus(es) is/are non-viable and is/are not expelled spontaneously from the uterus.

Modified natural cycle: an IVF procedure in which one or more oocytes are collected from the ovaries during a spontaneous menstrual cycle. Drugs are administered with the sole purpose of blocking the spontaneous LH surge and/or inducing final oocyte maturation.

Multiple gestation/birth: a pregnancy/delivery with more than one fetus/neonate.

Natural cycle IVF: an IVF procedure in which one or more oocytes are collected from the ovaries during a spontaneous menstrual cycle without any drug use.

Neonatal death: death of a live born baby within 28 days of birth.

Neonatal period: the time interval that commences at birth and ends 28 completed days after birth.

Oocyte donation cycle: a cycle in which oocytes are collected from a donor for clinical application or research.

Oocyte recipient cycle: an ART cycle in which a woman receives oocytes from a donor.

Ovarian Hyper Stimulation Syndrome (OHSS): an exaggerated systemic response to ovarian stimulation characterized by a wide spectrum of clinical and laboratory manifestations. It is classified as mild, moderate or severe according to the degree of abdominal distention, ovarian enlargement and respiratory, haemodynamic and metabolic complications.

Ovarian torsion: the partial or complete rotation of the ovarian vascular pedicle that causes obstruction to ovarian blood flow, potentially leading to necrosis of ovarian tissue.

Ovulation Induction (OI): pharmacological treatment of women with anovulation or oligo-ovulation with the intention of inducing normal ovulatory cycles.

Perinatal mortality: fetal or neonatal death occurring during late pregnancy (at 20 completed weeks of gestational age and later), during childbirth and up to 7 completed days after birth.

PESA: Percutaneous Epididymal Sperm Aspiration.

Post-term birth: a live birth or stillbirth that takes place after 42 completed weeks of gestational age.

Preimplantation Genetic Diagnosis (PGD): analysis of polar bodies, blastomeres or trophectoderm from oocytes, zygotes or embryos for the detection of *specific* genetic, structural and/or chromosomal alterations.

Preimplantation Genetic Screening (PGS): analysis of polar bodies, blastomeres or trophectoderm from oocytes, zygotes or embryos for the detection of aneuploidy, mutation and/or DNA rearrangement.

Preterm birth: a live birth or stillbirth that takes place after at least 20 but before 37 completed weeks of gestational age.

Recurrent spontaneous abortion/miscarriage: the spontaneous loss of two or more clinical pregnancies.

Reproductive surgery: surgical procedures performed to diagnose, conserve, correct and/or improve reproductive function.

Severe Ovarian Hyper Stimulation Syndrome: severe OHSS is defined to occur when hospitalization is indicated. (see definition of Ovarian Hyper Stimulation Syndrome)

Small for gestational age: birth weight less than 2 standard deviations below the mean or less than the 10th centile according to local intrauterine growth charts.

Sperm recipient cycle: an ART cycle in which a woman receives spermatozoa from a donor who is someone other than her partner.

Spontaneous abortion/miscarriage: the spontaneous loss of a clinical pregnancy that occurs before 20 completed weeks of gestational age (18 weeks post fertilization) or, if gestational age is unknown, the loss of an embryo/fetus of less than 400 grams.

TESA: Testicular Sperm Aspiration.

TESE: Testicular Sperm Extraction.

Total delivery rate with at least one live birth: the estimated total number of deliveries with at least one live born baby resulting from one initiated or aspirated ART cycle including all fresh cycles and all frozen/thawed ART cycles. This rate is used when all of the embryos fresh and/or frozen/thawed have been utilized from one ART cycles. *Note: The delivery of a singleton, twin or other multiple pregnancy is registered as one delivery.*

Vanishing sac(s) or embryo(s): spontaneous disappearance of one or more gestational sacs or embryos in an ongoing pregnancy, documented by ultrasound.

Very low birth weight: Birth weight less than 1,500 grams.

Very preterm birth: a live birth or stillbirth that takes place after at least 20 but less than 32 completed weeks of gestational age.

Vitrification: an ultra-rapid cryopreservation method that prevents ice formation within the suspension which is converted to a glass-like solid.

Zygote: a diploid cell resulting from the fertilization of an oocyte by a spermatozoon, which subsequently divides to form an embryo.

Zygote Intra-Fallopian Transfer (ZIFT): a procedure in which zygote(s) is/are transferred into the Fallopian tube.

References

- International Committee for Monitoring Assisted Reproductive Technology (ICMART): Adamson G.D., de Mouzon J., Lancaster P., Nygren K.G., Sullivan E., Zegers-Hochschild F. World Collaborative Report on *in-vitro* Fertilization, 2000. *Fertil Steril* 2006, **85**(6); 1586–1622.
- International Committee for Monitoring Assisted Reproductive Technology, de Mouzon J., Lancaster P., Nygren K.G., Sullivan E., Zegers-Hochschild F., Mansour R., Ishihara O., Adamson D. World Collaborative Report on *in-vitro* Fertilization, 2004. *Hum Reprod* 2009, in press.
- Dickey R.P. The relative contribution of assisted reproductive technologies and ovulation induction to multiple births in the United States 5 years after the Society for Assisted Reproductive Technology/American Society for Reproductive Medicine recommendation to limit the number of embryos transferred. *Fertil Steril* 2007, **88** (6); 1554–1561.
- The European IVF-monitoring (EIM) Consortium, European Society of Human Reproduction and Embryology (ESHRE). Assisted reproductive technology in Europe, 2004: results generated from European registers by ESHRE. *Hum Reprod* 2008, **23**; 756–771.
- Zegers-Hochschild F., Nygren K.G., Adamson G.D., de Mouzon J., Lancaster P., Mansour R., Sullivan E. on behalf of the International Committee Monitoring Assisted Reproductive Technologies (ICMART). The International Committee Monitoring Assisted Reproductive Technologies (ICMART) Glossary on ART Terminology. *Fertil Steril* 2006, **86** (1); 16–19.
- Zegers-Hochschild F., Nygren K.G., Adamson G.D., de Mouzon J., Lancaster P., Mansour R., Sullivan E. on behalf of the International Committee Monitoring Assisted Reproductive Technologies. The ICMART Glossary on ART Terminology. *Hum Reprod* 2006, **21**(8); 1968–1970. Epub 2006, Jul 24
- International Committee for Monitoring Assisted Reproductive Technology (ICMART). The ICMART Glossary. *Current practices and controversies in assisted reproduction. Report of a WHO meeting*. Geneva, Switzerland: World Health Organization, 2002; xix–xxi.