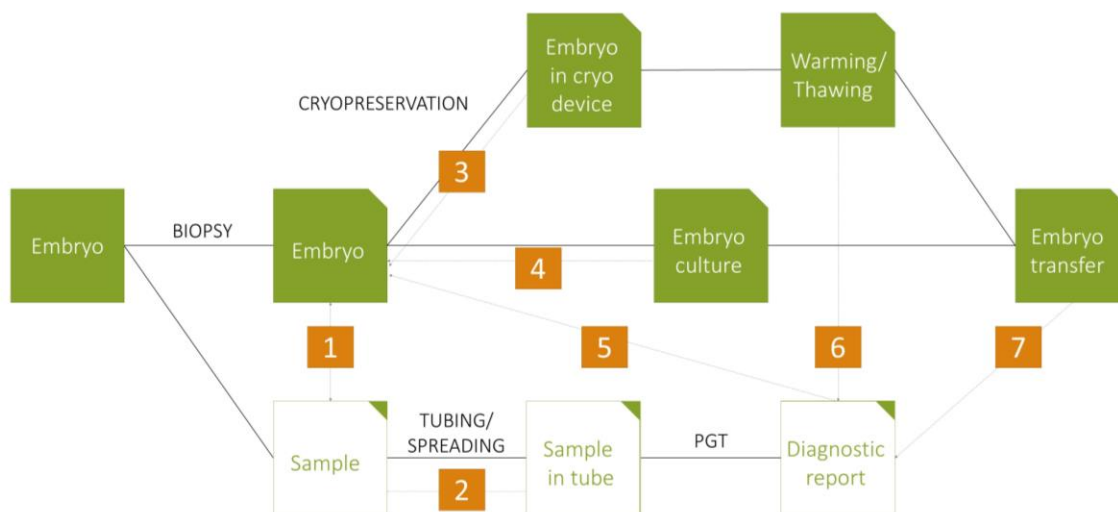
433 • The labelling system should be comprehensible and practical for both the IVF and the PGT
434 centre. Printed sticker labelling may be superior to pens as labelling should be legible and
435 inedible.
436 • Labelling and sample identification should be confirmed for critical and high-risk steps by an
437 independent observer and signed off (see figure 2). These critical steps are detailed in the
438 technical papers for the various methods (refer biopsy paper, PGT-M paper and PGT-A/SR
439 paper).
440 • After biopsy, the sample may be analysed in house, or sent for genetic testing in another centre
441 (see section 5. Transport PGT).

442 *Figure 2: outline of the biopsy and genetic testing procedure with indications of the 7 critical steps where*
443 *labelling and sample identification should be confirmed*



444

445 *Figure legend; Witnessing is recommended during the following stages: (1) Immediately after biopsy to*
446 *confirm the embryo and sample number match; (2) During spreading or tubing, to confirm that the*
447 *sample identification matches the labelling on the relevant slide or tube, respectively; (3) In case of*
448 *cryopreservation, immediately after biopsy before acquiring the genetic analysis results, at placing and*
449 *labelling the embryo into the cryopreservation device; (4) For further embryo culture, at placing and*
450 *labelling the embryo into the culture dish, and (5) When diagnostic results are issued to ensure accuracy*
451 *and correlation with the correct sample and/or embryo identification; (6) During the thawing/warming*
452 *procedure to ensure accuracy and correlation with the correct embryo diagnostic result; (7) At the time*
453 *of selecting the embryo(s) for embryo transfer.*

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455 # 4. PRECLINICAL WORK-UP, EXAMINATION AND POST-EXAMINATION PROCESS

456 ## 4.1 Preclinical work-up and validation

457 The PGT work-up report should contain at least the following information (Claustres *et al.*, 2014):

458 – administrative information:

459 - title or name of the report,
460 - number of the report (as used for document control, when available),
461 - pagination including the actual and total number of pages (The patient identifier
462 and report name/number must be present on each additional page),
463 - full date of the report,
464 - name and address of the physician referring the patient,
465 - identification of the person(s) performing the diagnosis/authorizing the release of
466 the report and their signature,
467 - identity of the IVF/PGT centre with full contact details.

468 - patient (male and female)/sample identification
469 - full given name(s) and surname, or unique patient identification code
470 - unequivocal date of birth
471 - gender

472 - specific for the preclinical work-up report:
473 - date of DNA sample collection,
474 - date of DNA sample arrival in the laboratory.

475 - restatement of the clinical question, i.e. the indication(s) being requested for analysis, the
476 type of required testing, the referral reason.

477 - specification of genetic tests used
478 - brief information on the methods used in the analysis,
479 - full details of the extent of the tests, including software, where appropriate,
480 - where a commercially available kit is used, this should be clearly identified in the
481 report, including the reference and version of the kit.

482 - a clear summary of the result

483 - error rates/limitations of the test/misdiagnosis (a general figure should be stated for the
484 overall cycle/treatment)

485 • It is recommended that all reporting based on haplotyping clearly states that the accuracy of
486 the results is based on the assumption that samples received were correctly identified, family
487 relationships are true and the clinical diagnosis of relatives is correct.

488 • It is recommended that any particularity of the protocol (e.g. specifying type of biopsy, number
489 of cells) is clearly indicated and communicated to both the patient and the IVF centre, if
490 needed.

491 ## 4.2 Examination process

492 • The examination process and reporting of results, must comply with local guidelines or law, or
493 with the ISO 15189 standard.

494 • Before starting a clinical PGT cycle, relevant documents should be available, labelling of
495 samples should be checked, and genetic counselling provided to the couple.

496 • It is recommended that the PGT laboratory has clearly documented procedures for all steps of
497 the examination process (explicit instructions and a summary of validation results) and release
498 of results (diagnosis, reporting, embryos transfer policy). These procedures are preferably
499 covered in a service level agreement between the PGT and IVF centres.

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- Many different methods have been published and all appropriately validated methods are acceptable for clinical cases. The method used should have been previously implemented, tested and validated in the PGT centre.

Scoring of clinical results

- It is recommended that results are reviewed and signed or electronically validated by a suitably qualified person (name, qualification, date).

Clinical cycle report

The PGT cycle report contains interpretation of the clinical results and guidance on which embryos are genetically transferable. The same recommendations apply as specified for the preclinical work-up report (see section 4.1), together with the following items:

  - unique cycle/treatment code
  - date of oocyte retrieval
  - date of biopsy
  - date of biopsy sample arrival in the laboratory
  - information on the sample type (including number of samples and controls)
  - unique ID number for each cycle and/or biopsy sample tested

- When scoring results from PB testing, it is recommended to report what was detected in each polar body and then infer the embryo diagnosis. It is recommended to test both PBs.
- When scoring results from blastomere/TE testing, it is recommended to report what was detected in the sample and then infer the embryo diagnosis.
- When results are reported from "pooling" of embryos, it is advisable to refer to each oocyte and sample collection date and clearly differentiate the embryo number between cycle/treatment.
- Reporting of clinical results to the IVF centre must follow local regulations or international accreditation guidelines, including general data protection regulations (GDPR).
- The embryo transfer policy should be agreed upon between stakeholders (IVF centre, genetic centre, genetic counsellors, clinicians and patients). In PGT-M and PGT-SR cases, embryos with no or inconclusive results are not recommended for transfer. Depending on local rules and following adequate counselling of the prospective parents, the carrier status of embryos (for autosomal recessive or X-linked recessive disorders) may be taken into consideration for embryo selection. In case of PGT-A in addition to PGT-M or PGT-SR, it is crucial to agree on a clear embryo transfer policy and a possible embryo ranking.
- A written or electronic report should be securely transmitted to the IVF centre to ensure transfer and/or cryopreservation of the correct embryos. Results should not be communicated orally.
- Reporting time should be kept as short as possible, and when fresh transfer is intended, the timing of the IVF centre should be taken into account.
- It is recommended that the report is clear, concise, accurate and easily understandable by non-geneticists.
- It is recommended that the overall result and interpretation is presented per embryo, preferably in tabulated form.

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- In case of no diagnosis and re-biopsy to try and obtain a result, this should be included in the report.
- The final clinical cycle report must be signed by appropriately qualified (authorized) personnel (name, qualification, date).
- It is recommended that the clinical cycle results are discussed with the couple before embryo transfer.
- It is recommended that the report is stored in the patient file in the PGT centre, according to local regulations.
- It is recommended to include a disclaimer in the report to address limitations of the test and any other information that may be of significance to the addressee.
- It is acceptable to indicate in the report the need for prenatal testing to confirm the result in case of pregnancy.

Further details on the specific reporting of the results and interpretation of results are outlined in the technical recommendations papers (refer PGT-M paper and PGT-A/SR paper)

4.3 Post-examination process

PGT cycle follow-up

For quality purposes, it is recommended to confirm the PGT diagnosis on embryos not transferred or cryopreserved following diagnosis, in line with local regulations. Such confirmation aims to provide ***quality assurance (QA)*** as well as accurate and up to date misdiagnosis rates to prospective PGT patients. It is recommended that this is performed on as many embryos as is practicable. It is acceptable to perform this periodically.

When a pregnancy ensues following PGT testing, it is recommended that parents are (again) made aware of the chance and risks of a misdiagnosis and be informed on the possibilities for prenatal testing. PGT and IVF centres should make special efforts to follow-up with the parents following prenatal testing or birth, especially if confirmatory testing is not possible.

Follow-up data should be used both for internal ***quality control (QC)***/QA purposes and documented in the ESHRE PGT Consortium online database for international data collection.

It is recommended that laboratories follow local regulations or accreditation schemes on storage of clinical samples and patient records.

If no local regulations or guidelines exists, it is recommended that:

- If embryos have been transferred and/or frozen, all relevant material (e.g. FISH slides, DNA amplification products) from the case should be retained and appropriately stored. Samples should be stored for at least 1 year. Prolonged sample storage could be considered taking into account the availability of information on delivery and the duration of embryo cryopreservation.
- If there is no genetically suitable embryo for transfer or cryopreservation, it is not necessary to keep the samples.
- If there is no pregnancy after transfer of all genetically suitable embryos, samples can be discarded.

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Misdiagnosis rate

- It is recommended that each PGT centre performs a prospective risk analysis in order to prevent and/or eliminate possible causes of ***misdiagnosis***.
- It is recommended that misdiagnosis rates should be calculated for each type of method and for all methods from a particular centre. Misdiagnosis rates include those clinical cases in which affected pregnancies arose and cases for which re-analysis results were discordant with the biopsy result.
- It is recommended that confirmatory testing should be performed at least periodically as a QA.
- It is recommended that the published and in-house estimates of misdiagnosis rates should be available on request to prospective patients along with pregnancy rates to allow informed consent for PGT.
- Following a misdiagnosis, the IVF/PGT centre should investigate the possible causes of the misdiagnosis and make changes to protocols to eliminate the risk in the future. Many of the causes of misdiagnosis are avoidable by taking preventative actions and following the principles of quality management.
- Misdiagnosis should be reported, for instance through the ESHRE PGT Consortium online database.

Baseline IVF pregnancy rates for PGT

- Setting appropriate baseline (ongoing) pregnancy rates should be left up to the individual centres. However, it is recommended that each IVF centre should compare PGT pregnancy rates and matched non-PGT (routine IVF or ***intracytoplasmic sperm injection (ICSI)***) pregnancy rates within that IVF centre.
- Comparison of pregnancy rates with those reported by the ESHRE PGT Consortium or comparable peers can also be carried out to set benchmarks for continual improvement of the PGT centre.

5. Transport PGT

- When in house genetic analysis is not feasible, transport PGT can be an option providing patients with IVF treatment (oocyte retrieval, embryo culture, biopsy and transfer, pregnancy follow-up) at their local IVF centre, which collaborates with a PGT centre with significant experience in genetic testing.
- The IVF centre and PGT centre should have in place an official agreement (Service Level Agreement) dealing with legal, insurance and accountability issues about the Transport PGT procedures.
- The IVF centre and PGT centre should make arrangements to ensure that patients have had adequate PGT counselling.
- The IVF centre and PGT centre should have in place a set of clinical/laboratory validated protocols, including tubing/spreading protocols, and shipment protocols specifying approximate transportation time and ensuring cell and/or DNA integrity.
- In addition, practical and logistic arrangements on who will be responsible for the various stages of the PGT treatment should be clearly established.

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620 - The IVF centre and PGT centre should delineate clear and sufficient lines of communication as
621 documented in written procedures and complying to the General Data Protection Regulation
622 GDPR during all stages of a transport PGT treatment.
623 - *Preclinical Runs*: before sending/receiving clinical samples from the treatment cycles, one or
624 more 'preclinical runs' are recommended. This practice may detect issues related to the quality
625 of biopsy, handling and labelling of biopsied samples, and the transport. Negative control
626 specimens should be included in preclinical runs to assess contamination. The sensitivity and
627 specificity of genetic testing should be evaluated and compared to in house samples and/or
628 samples received from other IVF centres. The reporting of the results should be agreed upon.
629 - The IVF/PGT centres should agree on the feasibility, the number and the timing of transport
630 PGT cycles, and define a schedule.
631 - It is recommended that all diagnostic results and reports are sent in written form (complying
632 to the GDPR).
633 - The IVF centre and PGT centre should agree on who is responsible for the collection of PGT
634 data and follow-up of PGT children (www.eshre.eu/data collection).

635 # 6. FOLLOW-UP OF PGT PREGNANCIES AND CHILDREN

636 ## 6.1 Prenatal diagnosis

637 Prenatal diagnosis should be offered to all women who become pregnant following PGT. The discussion
638 about the tests available should be undertaken by a suitably qualified professional to ensure that all
639 available options are presented, including invasive tests such as chorionic villus sampling and
640 amniocentesis, ultrasound scanning or non-invasive prenatal tests such as cell-free fetal DNA testing.

641 As an alternative to prenatal diagnosis, patients could choose to have postnatal confirmation by cord
642 blood sampling. However, testing of minors for late-onset conditions in the absence of a clinical benefit
643 is not recommended (Clarke, 1994).

644 ## 6.2 Follow-up of PGT pregnancies and children

645 There have been concerns about the health of children after assisted reproductive technologies (ART),
646 and in particular after embryo biopsy techniques and prolonged culture to blastocyst.

647 So far there is no indication that embryo biopsy causes an increased risk for adverse neonatal outcome.
648 However, PGT includes ART for which there is evidence that ART singleton children differ from
649 spontaneously conceived children. It is unclear whether this difference is due to the infertility status of
650 the couple and/or the ART procedure itself.

651 There is uncertainty about the long-term impact of ART and/or PGT and IVF/PGT centres should be
652 encouraged to obtain follow-up data on babies born after treatment, preferably in collaborative
653 prospective and retrospective studies. If this is not possible, the suggested minimum data set to collect
654 should include:

655 – date of birth,
656 – singleton versus multiple pregnancy + chorionicity status,
657 – gestational age at birth,

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658 – delivery mode,
659 – birthweight and length,
660 – sex,
661 – congenital abnormalities

662 Neonatal complications and APGAR score can additionally be recorded.

663 7. ACCREDITATION AND QUALITY MANAGEMENT

664 7.1 Accreditation

665 Accreditation, along with proficiency testing through internal (IQA) and external quality assessment
666 (EQA), provides a means to achieve and maintain the highest quality standards. Accreditation is the
667 formal recognition that an authoritative body gives to a laboratory/department/centre when it
668 demonstrates competence to carry out defined tasks and involves all aspects of management, along
669 with technical requirements.

670 Where possible, IVF/PGT centres should be accredited/certified, even when it is not legally required.

671 Because PGT is of a multidisciplinary nature, the various units involved should each be
672 accredited/certified for their defined tasks and according to the most appropriate quality standards.
673 For each unit, responsibilities should be clearly outlined/described and transition of responsibility from
674 one unit to the other during the PGT process should be well defined and guaranteed.

675 IVF/PGT laboratories should strive for accreditation conform the latest version of ISO15189 or
676 equivalent international/local standards and work with international diagnostic laboratory
677 accreditation schemes, if available.

678 IVF/PGT clinical units should strive for accreditation conform the latest version of ISO9001 or equivalent
679 international/local standards and work with medical/clinical peer review, if available.

680 7.2 Quality management

681 It is recommended that a ***quality management system*** is integrated to the IVF/PGT centre. Quality
682 management ensures that an IVF/PGT centre and the PGT service it provides, is of consistent quality. It
683 has four main components: quality planning, QA, QC and quality improvement. To most if not all
684 accreditation/certification schemes, QA and QC are prerequisites.

685 Aspects of quality management to be implemented include amongst others, quality policy, quality
686 manual, document control, compliance to SOPs, risk management, continual improvement, audits and
687 management review. Technical requirements include personnel, laboratory conditions and
688 environment, laboratory equipment, all stages of examination procedures, results reporting and QA.

689 • It is recommended that PGT centres participate on a regular basis in EQA schemes; GenQA
690 offers schemes for PGT that cover all types of analysis performed (https://www.genqa.org/).
691 • Validation of all methods used is recommended.

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692 • Written SOPs should be available for all steps of the PGT procedure. Laboratory staff should
693 have profound knowledge of the SOPs as these are the fundamental backbone of the service.
694 Deviations from protocols should be recorded.
695 • ***Risk assessment*** is part of the QC system and required for every stage of the PGT process. It
696 should be integrated into the SOPs.
697 • Laboratories should perform a risk assessment analysis to estimate the probability of a putative
698 hazard, the severity of their consequences, as well as the chances for detection of error. A
699 collaborative and multidisciplinary approach between the different operators involved in the
700 management of a PGT cycle would lead then to the prevention of any putative procedural risk
701 and implementation of specific corrective measures.

702

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SUPPLEMENTARY DATA 1. GLOSSARY

This glossary defines the most important terms used in the PGT papers and was developed to more easily understand the recommendations. Where appropriate, definitions were used as previously published, sometimes with adaptations to the context of PGT. Other definitions were derived from explanations within the context of the recommendations papers.

Term	Definition	Reference
Advanced maternal age (AMA)	Maternal age between 36-40 years	(Verpoest *et al.*, 2018)
Amplification bias	Artefactual duplications or deletions due to local concentration differences in guanine and cytosine bases (% G+C bias), as well as the prevalence of chimeric DNA molecules, allele drop outs (ADOs), preferential allelic amplifications and nucleotide misincorporations during amplification vary substantially between different WGA approaches. A major challenge in single-cell genome analysis is discriminating such WGA artefacts from genuine genetic variants present in the cell before WGA.	(Vermeesch *et al.*, 2016)
Allele drop out (ADO)	The failure to detect an allele in a sample or the failure to amplify an allele.	(Vermeesch *et al.*, 2016)
Allele drop in (ADI)	An allele which is detected, but is not actually part of the genotype, like a false positive.	
Assisted hatching	An ART procedure in which the zona pellucida of an embryo is either thinned or perforated by chemical, mechanical or laser methods.	(Zegers-Hochschild *et al.*, 2017)
B allele frequency (BAF)	The signal intensity of the B allele over the total signal intensity (A+B) for a SNP	
Blastocoele	Fluid-filled inner cavity of the blastocyst.	Adapted from (Zegers-Hochschild *et al.*, 2017)
Blastocyst	The blastocyst contains a fluid filled inner cavity (blastocoele), an outer layer of cells (trophectoderm) and an inner group of cells (inner cell mass). This stage of preimplantation embryo development occurs around Day 5–6, and occasionally Day 7 after ICSI.	Adapted from (Zegers-Hochschild *et al.*, 2017)
Blastomere	A cell from a cleavage-stage embryo.	Adapted from (Zegers-Hochschild *et al.*, 2017)
Cleavage-stage embryos	Embryos beginning with the 2-cell stage and up to, but not including, the morula stage.	(Zegers-Hochschild *et al.*, 2017)
Cryopreservation	The process of slow freezing or vitrification to preserve biological material (e.g. gametes, zygotes, cleavage-stage embryos, blastocysts or gonadal tissue) at extreme low temperature.	(Zegers-Hochschild *et al.*, 2017)
De novo segmental chromosome aberration in embryo	A segmental or partial chromosome deletion/ duplication arising in embryos of couples with normal karyotypes.	
Decontamination	The process of removing or neutralizing contaminants.	(Guide to the quality and safety of tissues and cellls for human application, 2017)

Denudation	The removal or stripping of the cumulus and corona cells from the oocyte.	Adapted from (Guide to the quality and safety of tissues and cellls for human application, 2017)
Sequencing read depth	A crucial parameter in sequencing referring to the number of times a particular read was found independently at a given genomic position.	
Developmental competence	Ability of an oocyte/embryo to complete preimplantation development to the blastocyst stage.	
Electronic witnessing system	Any automated electronic system that assists the traceability of the gametes/embryos in an IVF centre.	
Embryo biopsy	The removal of polar bodies, blastomeres or trophectoderm cells from the embryo for the purpose of genetic analysis.	(Guide to the quality and safety of tissues and cellls for human application, 2017)
Diploidy/euploidy	The condition in which a cell has two haploid sets of chromosomes. Each chromosome in one set is paired with its counterpart in the other set. A diploid embryo has 22 pairs of autosomes and two sex chromosomes, the normal condition.	Adapted from (Zegers-Hochschild *et al.*, 2017)
Exclusion testing	An optional add-on to genetic testing, where DNA from parents and grandparents is compared with the DNA of the embryo or fetus. Exclusion testing means that the at-risk parent doesn't have to have a presymptomatic genetic test to have disease-free children.	Adapted from https://huntingtonstudygroup.org/glossary/exclusion-testing/
Freeze-all cycle	An ART cycle in which, after oocyte aspiration, all oocytes and/or embryos are cryopreserved, and no oocytes and/or embryos are transferred to the uterus of a woman in that cycle.	Adapted from (Zegers-Hochschild *et al.*, 2017)
Genome coverage	the percentage of the target genome covered (in amplification or in sequencing)	
Hatching	The process by which an embryo at the blastocyst stage extrudes out of, and ultimately separates from, the zona pellucida.	(Zegers-Hochschild *et al.*, 2017)
High-order multiple gestation	A pregnancy with three or more embryos or fetuses.	(Zegers-Hochschild *et al.*, 2017)
Homoplasmy	A basic genetic state of mitochondria, in which all of the hundreds to thousands of mitochondrial (mt)DNA copies within a cell or an individual have the same nucleotide-sequence.	(Shibata and Ling, 2007)
Informativity testing	Genotyping of different loci within or flanking the region of interest using DNA from the couple and other relatives prior to segregation analysis for PGT-M preclinical process.	
Informed consent	A person's voluntary agreement based upon adequate knowledge and understanding of relevant information, to donate, to participate in research or to undergo a diagnostic, therapeutic or preventive procedure.	(Guide to the quality and safety of tissues and cellls for human application, 2017)
Inner cell mass (ICM)	A group of cells in the blastocyst that give rise to the embryonic structures and the foetus, the yolk sac, the allantois and the amnion.	(Guide to the quality and safety of tissues and cellls for human application, 2017)

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Intracytoplasmic sperm injection (ICSI)	A procedure in which a single spermatozoon is injected into the oocyte cytoplasm.	(Zegers-Hochschild *et al.*, 2017)
In vitro fertilization (IVF)	A sequence of procedures that involves extracorporeal fertilization of gametes. It includes conventional in vitro insemination and intracytoplasmic sperm injection (ICSI)	(Zegers-Hochschild *et al.*, 2017)
Log2 of fluorescence ratios	The log2 transformed value of the normalized signal intensity of a SNP. *(A logR of 0 and BAF values of 0, 0.5 and 1 represent a normal copy number (n=2). A single copy yields a logR of -1 and BAF values of 0 and 1, while 3 copies yield a logR of 0.58 and BAF values of 0, 0.33, 0.66 and 1)*	
Misdiagnosis	When a technical procedure has failed, is inaccurate or has been incorrectly interpreted. Misdiagnoses may be sample- or technique-specific.	Adapted from (Wilton *et al.*, 2009)
Monosomy	The absence of one of the two homologous chromosomes in embryos.	Adapted from (Zegers-Hochschild *et al.*, 2017)
Morula	An embryo formed after completion of compaction, typically 4 days after ICSI	Adapted from (Zegers-Hochschild *et al.*, 2017)
Chromosomal Mosaicism	A state in which there is more than one karyotypically distinct cell population arising from a single embryo.	(Zegers-Hochschild *et al.*, 2017)
Mutation	A permanent change in the nucleotide sequence, proven to be disease causing (class 4-5) and usually with a frequency below 1%.	(Richards *et al.*, 2015)
Negative control	The IVF laboratory negative control is a negative control with sample collection buffer, biopsy media, or washing media to control for contamination during each step of cell sample collection. The genetic laboratory negative control is a negative control with amplification mixture only to control for contamination during set-up of amplification reactions.	
Perivitelline space	The space between the cytoplasmic membrane enclosing the oocyte and the innermost layer of the zona pellucida. (This space may contain the first and second polar bodies and extracellular fragments)	(Zegers-Hochschild *et al.*, 2017)
Polar bodies (PBs)	The small bodies containing chromosomes segregated from the oocyte by asymmetric division during telophase. The first polar body is extruded at telophase I and normally contains only chromosomes with duplicated chromatids (2c); the second polar body is extruded in response to fertilization or in response to parthenogenetic activation and normally contains chromosomes comprising single chromatids (1c).	(Zegers-Hochschild *et al.*, 2017)
Polyploidy	The condition in which a cell has more than two haploid sets of chromosomes (f.x. a triploid embryo has three sets of chromosomes; a tetraploid embryo has four sets)	(Zegers-Hochschild *et al.*, 2017)
Preimplantation genetic testing (PGT)	A test performed to analyze the DNA from oocytes (polar bodies) or embryos (cleavage-stage or blastocyst) for HLA-typing or for determining genetic abnormalities. These include PGT for aneuploidies (PGT-A), PGT for monogenic/single gene defects (PGT-M), and PGT for chromosomal structural rearrangements (PGT-SR).	(Zegers-Hochschild *et al.*, 2017)
Quality assurance (QA)	The actions planned and performed to provide confidence that all systems and elements that influence the quality of the product are working as expected, both individually and collectively.	(Guide to the quality and safety of tissues and cellls for human application, 2017)

Quality control (QC)	The part of quality management focused on fulfilling quality requirements. In terms of preparation, it concerns sampling specifications and testing; for an organization, it relates to documentation and release procedures, which together ensure that the necessary and relevant tests have actually been carried out and that materials have not been released for use until their quality has been judged to be satisfactory.	(Guide to the quality and safety of tissues and cellls for human application, 2017)
Quality management system	The organizational structure, with defined responsibilities, procedures, processes and resources, for implementing quality management, including all activities that contribute to quality, directly or indirectly.	(Guide to the quality and safety of tissues and cellls for human application, 2017)
Recurrent implantation failure (RIF)	Three or more failed in vitro fertilization-embryo transfer cycles involving high-quality embryos	Adapted from (Harper *et al.*, 2010)
Recurrent miscarriage (RM) / Recurrent pregnancy loss	Two or more pregnancy losses until 24 weeks gestation (including chemical pregnancy)	(RPL *et al.*, 2018)
Risk assessment	Identification of potential hazards with an estimation of the likelihood that they will cause harm and of the severity of the harm should it occur.	(Guide to the quality and safety of tissues and cellls for human application, 2017)
Segregation testing	Phasing or haplotyping (determination of the group of alleles within a genetic segment on a single chromosome being inherited together) after informativity testing to establish the high-risk and low-risk haplotypes	
Severe male factor (SMF)	Sperm sample with a combination of oligospermia (low sperm concentration), asthenozoospermia (poor sperm motility) and/or teratozoospermia (abnormal sperm morphology) or azoospermia.	Adapted from (World Health Organization, 2010)
Sexing	Selection of embryos based on sex	
Standard operating procedure (SOP)	Written instructions describing the steps in a specific process, including the materials and methods to be used and the expected result.	(Guide to the quality and safety of tissues and cellls for human application, 2017)
Sub-optimal environmental conditions	Any deviation from the theoretical physiological pH, temperature, oxygen level, or osmolarity.	
Supernumerary embryos	Excess embryos after embryo transfer.	(Guide to the quality and safety of tissues and cellls for human application, 2017)
Trisomy	An abnormal number of chromosome copies in a cell characterized by the presence of three homologous chromosomes rather than the normal two.	Adapted from (Zegers-Hochschild *et al.*, 2017)
Trophectoderm	Cells forming the outer layer of a blastocyst that have the potential to develop into the placenta and amniotic membranes.	(Zegers-Hochschild *et al.*, 2017)
Time-Lapse imaging	The photographic recording of microscope image sequences at regular intervals in ART, referring to gametes, zygotes, cleavage-stage embryos or blastocysts.	(Zegers-Hochschild *et al.*, 2017)
Uniparental disomy (UPD)	The presence of two copies of (part of) a chromosome, from one parent and no copy from the other parent.	(Vermeesch *et al.*, 2016)

Validation	Documented evidence giving a high degree of assurance that a specific process or system, including pieces of equipment or the environmental conditions, will perform consistently to deliver a product meeting its pre-determined specifications and quality attributes, based on intended use.	(Guide to the quality and safety of tissues and cellls for human application, 2017)
Vitrification	An ultra-rapid cryopreservation procedure that prevents ice formation within a cell whose aqueous phase is converted to a glass-like solid.	(Zegers-Hochschild *et al.*, 2017)
Zona pellucida	The glycoprotein coat surrounding the oocyte and the developing embryo up to the blastocyst stage	Adapted from (Zegers-Hochschild *et al.*, 2017)

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SUPPLEMENTARY DATA 2. LIST OF ABBREVIATIONS

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Abbreviation	Full term
aCGH	Array-based comparative genomic hybridization
ADI	Allele drop in
ADO	Allele drop out
AF	Amplification failure
AMA	Advanced maternal age
BACs	Bacterial artificial chromosomes
BMI	Body mass index
bp	Base pairs
DAPI	4′,6-diamidino-2-phenylindole, is a fluorescent stain that binds strongly to adenine–thymine rich regions in DNA
D-ARMS	Double amplification refractory mutation system
dNTPs	Deoxyribonucleotide triphosphates
EQA	External quality assessment
FISH	Fluorescence in situ hybridization
FM	Flanking marker
GDPR	General data protection regulations
HEPES	4-(2-hydroxyethyl)-1-piperazineethanesulfonic acid (buffering agent)
HGVS	Human genome variation society
HLA	Human leukocyte antigen
HS dsDNA	High sensitivity double stranded DNA
ICM	Inner cell mass
ICSI	Intracytoplasmic sperm injection
IQA	Internal quality assessment
ISCN	International system for human cytogenetic nomenclature
IVF	In vitro fertilization
Mb	Mega-bases
MDA	Multiple displacement amplification
MOPS	3-(N-morpholino) propane sulfonic acid (buffer)
mtDNA	Mitochondrial DNA
NGS	Next generation sequencing
PB	Polar body
PCR	Polymerase chain reaction
pg	Picogram
PGD	Preimplantation genetic diagnosis
PGS	Preimplantation genetic screening
PGT	Preimplantation genetic testing
PGT-A	PGT for aneuploidy
PGT-M	PGT for monogenic/single gene defects
PGT-SR	PGT for chromosomal structural rearrangements
QA	Quality assurance
QC	Quality control
QMS	Quality management system
qPCR	Quantitative real-time PCR

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RIF	Recurrent implantation failure
RM	Recurrent miscarriage
SBR	Signal to background noise ratio
SMF	Severe male factor
SNP	Single nucleotide polymorphism
SOP	Standard operating procedure
STR	Short tandem repeat (markers)
TE	Trophectoderm
UPD	Uniparental disomy
UPS	Uninterrupted power supply
UV-C	Ultraviolet C
WGA	Whole genome amplification
ZP	Zona pellucida

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