

# Traceability in IVF depends on each of us

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## Summary

**Introduction:** in IVF, one of the worst irreversible clinical risks is to obtain a pregnancy from an embryo produced from wrong gametes. Each infertility clinic, and in particular IVF lab, must create and apply rigorous procedures of traceability to avoid mismatch. We assessed the risk of patient/gamete/embryo traceability failure from gametes donation to processing, storage and distribution of embryos in a routine IVF protocol.

**Material and Methods:** the failure mode and effect analysis (FMEA) and critical analysis (FMECA) of each phase and under-phase of patient/gamete/embryo traceability in a routine IVF protocol, were performed by an internal multidisciplinary team.

**Results:** after critical analysis, the risk priority number score decreased from 8.1 to 3.8. There was no relevant risk of cell mismatch. Improvements were made to ensure the traceability of *in vitro* treatment and to avoid patient data cancellation on sperm collection container. Active witnessing was also imple-

mented.

**Conclusion:** the FMEA/FMECA methodology is an effective way to proactively assess the risk of traceability failure in IVF. Procedures can always be improved. The efficacy of patient/gamete/embryo traceability depends on each operator in the IVF unit. Each operator must be aware of their own role and responsibility in the traceability process.

**KEY WORDS:** FMEA, IVF, mismatch, risk assessment, traceability.

## Introduction

The European directives 2004/23/EC, 2006/86/EC, 2006/17/EC were received with the Italian legislative decree n. 16/2010 (1-4). The necessity to trace all the tissues and cells obtained, processed, stored or distributed from the donor (inside or outside the couple) to the recipient and vice versa was underlined. In the same European texts, serious adverse events and reactions were defined, or how an untoward occurrence may generate an unintended response from the patient associated with life-threatening, disabling, incapacitating condition or which results in, or prolongs, hospitalisation or morbidity. This corresponds to the definition of clinical risk according to Kohn (5).

In IVF, one of the worst irreversible clinical risks is a pregnancy from an unwanted embryo. The embryo production from wrong gamete(s) and/or its transfer in the wrong uterus has terrible human consequences. It is well known that these adverse events and reactions are due to patient, gamete or embryo traceability failure (6). In order to nearly erase the probability of this event, each IVF clinic and in particularly IVF lab must apply rigorous protocols of human cell traceability from gamete donation to gamete/embryo processing, storage and distribution. On the other hand, the risk assessment of each

traceability procedure must be tested to quantify its efficacy. The failure mode and effect analysis (FMEA) followed by critical analysis (FMECA) is a well-known methodology to proactively evaluate the efficacy of a health process (7).

In this study, we present the results of FMEA/FMECA analysis of our procedures regarding patient, gamete and embryo traceability in a routine IVF protocol. The scores were calculated on the retrospective data generated from the moment when the traceability procedures tested by FMEA/FMECA analysis were in use. Our results were included in the multicentre study designed by the Italian Society of Embryology Reproduction and Research (SIERR) in collaboration with the National Transplant Centre (CNT, Superior Institute of Health, Rome, Italy) and including other six Italian IVF centres.

## Materials and methods

### *Study design*

A multidisciplinary team of all professional figures involved in the processes was formed. All the patient/gamete/embryo traceability procedures in the IVF unit were analysed. The mismatch risks were proactively estimated making the calculation from the real probability of the adverse event to occur from the moment when the tested traceability procedures were in use, the detection mode applying the standard operation procedures in use at the moment of FMEA analysis, and the severity of the event as established in Table 1.

### *FMEA team*

The FMEA team was formed of seven internal members representing the professional figures involved in the entire traceability process: the laboratory director, that was also the Quality Control and Quality Assurance responsible, one embryologist specialized in IVF lab, one embryologist specialized in cryopreservation, two gynaecologists, one nurse and one medical secretary. The seven members analysed together the traceability process in a routine IVF protocol. An external specialist in risk assessment was present during FMEA/FMECA analysis.

### *Analysed processes and ongoing traceability protocols at the moment of FMEA analysis*

The IVF protocol was divided in the following

phases: oocyte collection, sperm collection (ejaculated and surgical sperm extraction), gamete processing, *in vitro* insemination (IVF or ICSI), embryo culture and transfer, and gamete and embryo cryopreservation. Each phase was analysed for infertile couples using their own gametes and without embryo genetic analysis. More than 6000 processes were analysed. Two operators were involved in the traceability processes performed in the IVF laboratory and cryo-zone area, and no less than four operators were involved in traceability processes performed in the IVF laboratory and theatre (oocyte collection, surgical sperm extraction, embryo-transfer). The traceability process and the participants involved are represented in Figure 1.

In our unit, patient identification was performed asking the patient to give data on couple identity (names, surnames, ID, dates of birth) and data were cross-checked with identity document and clinical records by an operator prior to semen production and at the moment of semen delivery for ejaculated sperm; before entering and inside the theatre for surgical sperm extraction patient and female patient before oocyte pick-up (OPU) and embryo transfer. Patient identification by multi-disciplinary team meant filling and signing of a specific form by each operator before OPU, embryo-transfer and surgical sperm extraction (clinician, biologist, nurse and anaesthetist when present).

In all IVF phases (gamete collection, cell culture and storage, embryo transfer, cell freezing and thawing), any container (tube, dish, pot, straw, vial) was labelled with patient/couple data before the cells were placed in it. The correspondence of cell data on the containers was double-checked before and after cell placement by the operator and a witness qualified to witness.

In the IVF lab, each time a cell was changed of place (tube, dish, pot, straw, vial, incubator, tank) or transferred (gamete/embryo) the procedure was double-checked by the operator and a witness qualified to witness. Each phase of the entire cell traceability process was recorded on a specific lab register and signed by the operator and the witness.

Each procedure performed in the theatre and the IVF lab was completed once the final checklist was filled and signed by the operator(s) and witness.

According to the under-phases, printed or hand written labels were used.

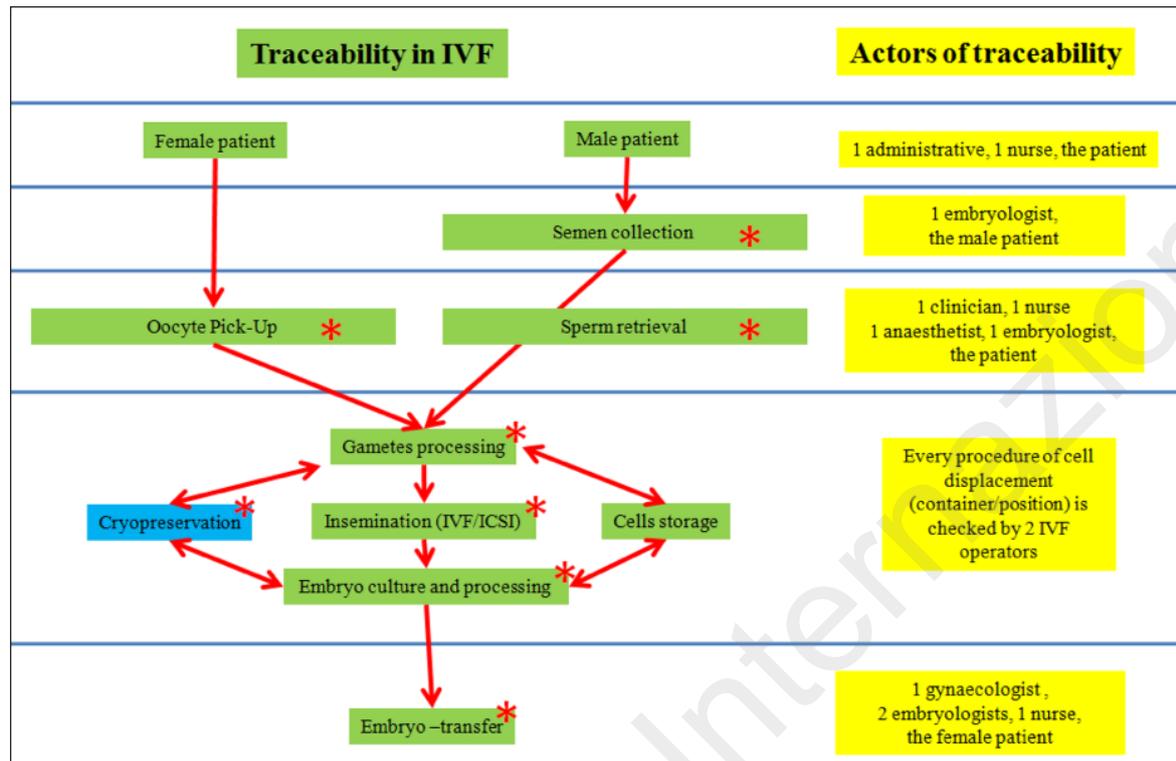


Figure 1 - Schema of traceability in IVF with the actors involved in this process.

\* The analyzed phases.

### FMEA analysis

The predefined FMEA team accurately reviewed the phases of patient/gamete/embryo traceability process in a routine IVF protocol. Each phase was sectioned in under-phases, analysed in detail and the risk priority number (RPN) score was calculated in accordance with each member of the FMEA team. RPN score was the result of the multiplication of occurrence probability (O), severity of impact on the process (S) and the chance of detection (D) ( $RPN=O \times S \times D$ ). We applied the scoring system in agreement with the other six infertility clinics involved in SIERR-CNT multicentre study (Table 1).

RPN score between 1-15 was considered a low risk of failure, 15 to 49 as moderate and superior to 49 as high. After FMEA analysis, propositions were made to modify the processes in a view to decrease RPN where necessary.

### Results

The analysed phases of traceability process were: oocyte collection (from patient identifica-

tion to oocyte culture); sperm collection (from patient identification to ejaculated semen collection or surgical sperm extraction and culture); oocytes and sperm processing for standard IVF or ICSI (oocyte culture and denudation for ICSI); insemination by standard IVF or ICSI; embryo culture and processing (incubator and/or culture dish change); embryo transfer and gamete/embryo cryopreservation. The 7 phases were divided in 27 under-phases and analysed in 50 steps tracing patient/gamete/embryo in a routine IVF protocol (Table 2).

The RPN score mean of traceability process in IVF was 8.1 after FMEA and decreased to 3.8 after FMECA. The highest RPN score 75 was obtained in oocyte processing and *in vitro* insemination due to the same traceability failure. It was a failure of treatment identification. Theatre and IVF laboratory activities follow the operating list established by medical and paramedical operators the day before activity. This operating list contains data of couples/patients to treat (ID, names, surnames, etc.) and the specific *in vitro* treatment to apply (IVF or ICSI). If standard IVF treatment is written instead of ICSI, the lab operator taking in consideration only

Table 1 - Scoring system for calculation of the probability of occurrence (O), severity (S) and detection (D) for each analysed process.

	Score	Rating	Description
O: occurrence	1	remote	Failure unlikely to occur, in $\leq 1/10,000$ IVF cycles
	2	low	relatively rare, from 1/9999 to 1/1000 IVF cycles
	3	moderate	occasional, from 1/999 to 1/300 IVF cycles
	4	high	recurrent, from 1/299 to 1/100 IVF cycles
	5	very high	common failure, in $> 1/99$ IVF cycles
S: severity	1	remote	no injury for gametes, embryos or patients
	2	low	Temporary injury needing additional intervention
	3	moderate	Temporary injury with potential reduction in the efficacy of the treatment
	4	high	Permanent effect on gametes and embryos
	5	very high	Permanent effect on patients
D: detection	1	very high	probability of detection 99-100% IVF cycles
	2	high	probability of detection 85-98% IVF cycles
	3	moderate	probability of detection 16-84% IVF cycles
	4	low	probability of detection 1-15% IVF cycles
	5	remote	probability of detection $< 1\%$ IVF cycles

Table 2 - FMEA analysis results of each phase and under-phase of routine IVF protocol and FMECA modification.

Process-phases	Number under-phases	Number of analysed steps	RPN score mean at FMEA [range]	RPN score mean after FMECA [range]
Oocyte collection	4	11	5.3 [2;10]	3.5 [2;6]
Oocytes processing	2	2	39.5 [4;75]	7 [4;10]
Sperm collection	8	18	6.4 [2;16]	3.6 [2;6]
In vitro Insemination	2	2	40 [5;75]	7.5 [5;10]
Embryo culture	2	2	2.5 [2;5]	2.5 [2;5]
Embryo transfer	3	6	4.8 [2;6]	4.3 [2;6]
Gamete and embryo freezing	3	6	4.3 [2;12]	2.8 [2;4]
Gamete and embryo thawing	3	3	3.7 [2;5]	3.7 [2;5]

RPN: risk priority number.

this operating list would perform standard IVF with a high risk of fertilization failure in case of very low semen quality or previous unexplained fertilization failure. Beside the barriers that already exist (the possibility for the lab operator to verify patient treatment using the centralised in-

formation system and other), we urged the operators responsible for the writing of operating list to define and apply a more effective procedure to establish and distribute an ultimate updated version. The writing operators had to verify, sign and successively distribute the operating list.

The second highest RPN score 16 was obtained in sperm collection. In a first moment, the nurse wrote the couple data on the semen collection container before ejaculated semen collection, reading identity document and clinical records and successively asking the patient to confirm data on the container. In case of cancellation of data on the container by the patient during semen production, the IVF lab personal could fail to identify the sample and eliminate it even if the sample was delivered by the patient himself. A second sample would be asked to the patient. This fact is embarrassing and could compromise the treatment if no spermatozoa is recovered in the second sample using a newly labelled semen collection container. The corrective measure we took was the following: the nurse asks the patient to identify himself (names, surnames, ID, data of birth of the couples) and confirms data said by the patient reading identity and clinical records, writes the couple data on the container, covers the written data with *transparent adhesive tape* to avoid data cancellation at the moment of semen production, makes the patient read and confirm the correctness of data written on the container and finally gives the container to the patient for semen production. At the moment of semen delivery to IVF lab personal, the lab operator identifies the patient asking him the same data written on the container and compares data with those of the operating list. At this point the lab operator confirms (or not) the exactness of the data.

The FMEA analysis of the other phases of IVF processes, did not show the need of urgent intervention. However, we made some improvements on traceability protocols and some RPN scores decrease after FMECA. One of those improvements was the active witnessing of the second operator. Before FMEA/FMECA analysis and at the moment of cell placement, the second operator read the cell data on the first dish where the cells were placed, and the second dish where the cells were going to be placed remaining quiet if something was wrong. Now the witnessing is active. The witness reads out loud and confirms cell data on the first dish where cells are placed and on the second dish where cells are going to be placed. The same witnessing protocol is applied each time the cells are changed of place (tube, dish, pot, straw, vial, incubator, tank) or transferred (gamete, embryo).

## Discussion

After FMEA/FMECA analysis of our entire IVF processes regarding patient/gamete/embryo traceability, the risk of patient/cell mismatching resulted low and no special improvement seemed to be needed. The same conclusion was found in gamete/embryo cryopreservation process. In our procedures, multiple patients and cell identification checkpoints were already active. We had known for a long time that name/surname identification mode is not sufficient because of the homonymy recurrence in surrounding territory, especially on an island. The main traceability failure regarded 'treatment traceability'. We considered as severe the possibility of treatment error. The application of standard IVF instead of ICSI due to a wrong treatment transcription in the IVF operating list could lead to embryo formation failure and transfer. If the couple victim of this mistake has a very limited remaining fertility reserve, the chances to obtain a pregnancy could be dramatically decreased. We modified our procedure to guarantee the distribution of the ultimate updated operating list to decrease the risk of treatment traceability failure. The other improvement thanks to FMEA/FMECA analysis was about the possibility of data cancellation on semen collection container.

Beside the process phases where a prompt corrective measure was required, some improvements were made, such as the 'active witnessing' from the second operator or the patient. We must never forget that one of the biggest fears of the IVF couple is gamete/embryo mismatch. Making the patients involved in cell traceability should comfort them that each operator recognized and recorded their identity. At the same time, the signature of each operator identifying the patient/cells should make the operator conscious that his own responsibility is fully engaged in the traceability process of the present case. On the other hand, it can be thought that an automated system would make the operator less involved and the process less controlled.

It is interesting to note that even if handwritten labelling is known to be an elevated potential source of error, no mismatch due to handwriting error was recorded. The reason may be that the operator writing the patients data on a support is witnessed by a second operator at this precise

moment. This way, we also eliminated the management protocol of labels that is obligatory in a pre-printed labelling system.

Two previous Italian studies reported their own results after FMEA/FMECA analysis of traceability processes (8, 9). Electronic witnessing system is a solution to eliminate the mandatory witness operator. Nevertheless, it cannot be applied for freezing procedures and has limitations for single gamete/embryo traceability. In these processes, the second operator witnessing is only applicable.

At the moment, we did not find the necessity to use an automated system of traceability. We feel comfortable with the human witnessing. Human witnessing requires human resources that can be missing in an IVF laboratory. Each director of IVF laboratory must establish procedures in which the moment of double-checking is precisely defined and recorded.

In a quality management system, improvements are mainly made on patient satisfaction and the analysis of events non-complying with what was expected. This methodology does not consider the near-missing events and does not study an entire process on a multidisciplinary vision like the clinical risk concept. The FMEA/FMECA methodology proactively analyses a process by a team involving all the figures present in a specific process. Root cause analysis can also be applied. It must be emphasized that the efficacy of a process depends on all the professional figures involved in the process and their own sense of responsibility in the application of the procedures. On the other side and during risk assessment analysis the multidisciplinary team must consider that any exception or unlikely accidental event may happen. In IVF, the patient/gamete/embryo traceability process is such a delicate issue that several figures are required.

We presented here the patient/gamete/embryo traceability process in an IVF block. The traceability efficacy depends on patient registration before IVF treatment. It is reminded that patient and gamete traceability find a particular importance in those IVF treatments using cells produced outside of the couple.

In our centre the traceability instruction processes are described in a manual common to all operators. The first procedure described is 'patient registration' at the first appointment. Each professional figure is informed of the entire pa-

tient/gamete/embryo traceability procedure and the specific place where he/she is involved. We recommend the adoption of a unique traceability manual. In this way, each operator understands better their own role and responsibility in the process, when it starts and ends. In our clinic, before applying a specific traceability procedure, it is presented and discussed with all the staff during a general meeting. The success of IVF traceability and patient wellbeing lays in the involvement of each member of the IVF centre. The IVF traceability can be guaranteed only if each actor understands and applies the procedure as it must be. Each time a procedure is even partially modified, the traceability process must be reanalysed and the mismatch risk reassessed.

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