Failure mode and effect analysis (FMEA) focused on traceability during IVF

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Summary

Failure Mode and Effect Analysis (FMEA) is a proactive technique for error detection and reduction. This study is a part of a multicenter and multidisciplinary Italian study led by Italian National Transplant Center, CNT Superior Institute of Health, Rome. The Authors have experimented the application of the Failure Mode and Effect Analysis (FMEA) technique in assisted reproduction cycles, focused on traceability during In Vitro Fertilization (IVF). A significant reduction of the risk priority number (RPN) was obtained when applying FMEA to the most vulnerable processes.

KEY WORDS: IVF, FMEA, traceability.

Introduction

Assisted reproductive treatment (ART) procedures and In Vitro Fertilization (IVF) treatments are characterized by high risk and complexity due to timing control, personnel's stress and work overload. For this reasons ART procedures need to be strictly linked to a strong quality control and quality assurance management program, which define protocols and procedures to reduce probability of error.

To minimize the risk of error during identification of patients and cell manipulation, an effective and accurate traceability system is mandatory (1).

The European Society of Human Reproduction and Embryology (ESHRE) developed the current clinical practice guideline, to provide clinical recommendations to improve the quality of healthcare delivery within the European field of human reproduction and embryology (2). In this document the Authors underline that a proactive risk assessments should be made and preventive actions taken to minimize non-conformities.

Failure modes and effects analysis (FMEA) is a step-by-step approach for identifying all possible mistakes that may occur during a process or service.

“Failure modes” means the ways, or modes, in which something might go wrong. Failures are any errors or defects, especially ones that affect the customer, and can be potential or actual.

“Effects analysis” refers to studying the consequences of those failures.

FMEA is a systematic, proactive method for evaluating a process to identify where and how it might fail and to assess the relative impact of different failures, in order to identify the parts of the process that are most in need of change.

FMEA includes review of the following: steps in the process, failure modes (what could go wrong?), failure causes (why would the failure happen?) and failure effects (what would be the
consequences of each failure?). Staff working in IVF center can use FMEA to evaluate ART processes for possible failures to prevent them by correcting the processes proactively, rather than reacting to adverse events after failures have occurred. This emphasis on prevention may reduce risk both for patients and staff.

**Material and methods**

This study takes place at Infertility Unit of the Fondazione IRCCS Cà Granda Ospedale Maggiore Policlinico of Milan, Italy. Our unit performs over 1000 IVF cycles per year and the team is composed by 39 persons (gynecologists, embryologists, nurses, administrative personnel). From April to September 2016 a multidisciplinary working group, instructed by proactive risk analysis, composed by 3 embryologist (including the quality management and quality assurance manager), 1 gynaecologist and 1 nurse, tested the traceability system of the Infertility Unit following FMEA analysis as described in the steps below:

1. Identify the objective of the FMEA, which is the traceability process related to IVF treatments, and how detailed should be, with a flowchart to describe the route;
2. Identify the main phases and, for each phase, identify the processes;
3. For each process, identify all the ways failure could happen;
4. For each failure mode, identify all the causes and the potential effects of failure;
5. For each cause, identify current process controls, for example SOP (standard operating procedures);
6. Determine how serious each effect is. This is the severity rating (S). Severity is usually rated on a scale from 1 to 5, where 1 is insignificant and 5 is catastrophic (3). On the FMEA table, list the severity rating for each cause. Severity was scored as followed: no injury for gametes, embryos or patients (score 1); temporary injury needing additional intervention (double check; delay in the procedure) (score 2); temporary injury with potential reduction in the efficacy of the treatment (partial loss of material) (score 3); permanent effect on gametes and embryos (complete loss of material) (score 4); permanent effect on patients (gametes or embryos mismatch) (score 5);
7. Determine the occurrence rating (O). This rating estimates the probability of failure occurring for that reason during the lifetime of your scope. Occurrence is usually rated on a scale from 1 to 5, where 1 is extremely unlikely and 5 is inevitable. On the FMEA table, list the occurrence rating for each cause. Occurrence was scored as follows: remote occurrence (score 1), failure unlikely to occur, in ≈1/10,000 IVF cycles; low occurrence (score2), relatively rare, in ≈1/1000 IVF cycles; moderate occurrence (score 3), occasional, in ≈ 1/200 IVF cycles; high occurrence (score 4), recurrent, in ≈1/100 IVF cycles and very high occurrence (score 5), common failure, in ≈1/20 IVF cycles;
8. Determine the detection rating (D). This rating estimates how the controls can detect either the cause or its failure mode after they have occurred but before the customer is affected. Detection is usually rated on a scale from 1 to 5, where 1 means the control is absolutely certain to detect the problem and 5 means the control is certainly not to detect the problem (or no control exists). On the FMEA table, list the detection rating for each cause. Detection was scored as follows: very high: probability of detection 100% (score 1), high: probability of detection ≈70% (score 2); medium: probability of detection ≈40% (score 3), low: probability of detection ≈10% (score 4); remote: probability of detection ≈1% (score 5);
9. Calculate the risk priority number or RPN, which equals S × O × D. An RPN between 1 and 15 was considered a low risk of failure, between 15 and 50 a moderate risk and over 50 a high risk of failure;
10. Identify recommended actions. These actions may be designed or processed changes to lower severity or occurrence. They may be additional controls to improve detection.

**Results**

The IVF team has identified eight main process phases: oocyte collection, sperm donation, gamete processing, insemination, embryoculture, cryopreservation and transport. PGD cycles are excluded from this analysis.
A total of 20 processes are listed (Table 1): patient registration and identification, medical chart opening and recovery, patient identification (bracelet) before the access at pick-up room, patient identification in the laboratory at the pick-up (daily scheduled program and biological record), identification of culture dishes and storage position inside the incubators, pick-up execution, registration and identification of the patient for semen collection, preparation of the recipient for semen collection with attached an “identification tag”, patient identification and check of the correspondence between seminal fluid collected, patient identity and self-certification, transfer of the seminal fluid from the recipient to the tube with attached the “identification tag”, oocyte denuding, maturity classification and use, identification of the right correspondence between gametes of the couple during insemination (matching), identification of culture dishes and storage place inside the incubators, association between embryos, culture dishes and storage position inside the incubators, patient registration and identification, medical chart opening and recovery, patient identification (bracelet) before the access at pick-up room, association between transfer embryos, transfer culture dishes and storage position inside the incubators, patient identification during embryo transfer in the laboratory (daily scheduled program and biological record), identification of the correspondence between gametes/embryos and cryopreservation device, identification of the correspondence between cryopreserved material and storage position, identification of the subject/couples responsible of the transport and identification of the correspondence between the cryopreserved sample and the storage position. All phases and processes are potentially exposed to mistakes in the traceability system and 35 failure modes have been identified (Table 1). The highest RPN is 25 (Table 1) and the most vulnerable processes are:

- gamete collection execution (pick up) without a correct check; failure mode: failure to verify the presence of tubes before pick up execution (double fault);
- identification of the correspondence between gametes/embryos and cryopreservation device; failure mode: incorrect association between embryos/gametes and devices.

For the first process (gamete collection execution) the team has suggested a revision of the procedure to reduce the RPN.

The IVF team has recognized that the possible causes of failures are mainly associated with heavy clinical workload and distraction, communication failures between the team and inadequacy of the labelling system used.

The most common effect is a procedural delay. The team has pointed out the key role of double check (witness) and its importance in the traceability system to prevent the risk of failure.

Witnesses are biologists or biotechnologists who oversee the critical steps: labelling at the time of oocyte retrieval, patient identification at the moment of sperm collection and sample processing, identification of the culture dish during the embryo culture, patient identification and sample processing in the embryo transfer, and identification of the correct biological sample when freezing/thawing gametes and embryos.

**Discussion**

The complexity of IVF treatments in these last years has forced to implement many different control measures to reduce the risk of failure.

The Human Fertility and Embryology Authority (HFEA) has published reports on the number of incidents involving IVF clinics in the United Kingdom (5, 6). They defined an “adverse incident” as: “[…] any event, circumstance, activity or action which caused, or had been identified as potentially causing, harm, loss or damage to patients, their embryos and/or gametes, or to staff or a licensed centre. This included serious adverse events, adverse reactions, breaches of confidentiality, and OHSS, which required a hospital admission and had a severity grading of severe or critical.” (7).

Diverse method exists to perform a risk analysis. For example the Root Cause Analysis (RCA) is a problem solving method used for identifying the root causes of faults or problems after their occurrence. A factor is considered a root cause if, after being taken off from the problem-fault-sequence, it prevents the final undesirable event from recurring.

FMEA system applied to IVF cycles requires to imagine how a process may fall, before it hap-
### Table 1 - FMEA Infertility Unit Policlinico Milan

<table>
<thead>
<tr>
<th>PHASES</th>
<th>PROCESSES</th>
<th>FAILURE MODE</th>
<th>CAUSES</th>
<th>EFFECTS</th>
<th>SOP</th>
<th>S</th>
<th>O</th>
<th>D</th>
<th>RPN</th>
<th>ACTIONS</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Oocyte collection</td>
<td>Patient registration and identification: medical chart opening and recovery</td>
<td>Incorrect completion of personal data (identification tag and hospitalization number)</td>
<td>Distraction / work overload</td>
<td>Procedural delay</td>
<td>P.12.732 &quot;Prendere degli avvisi&quot;</td>
<td>2</td>
<td>2</td>
<td>1</td>
<td>4</td>
<td>Procedure ID, worklist evaluation</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Incorrect completion of personal data (identification tag and hospitalization number)</td>
<td>Distraction</td>
<td>Procedural delay</td>
<td>P.12.732 &quot;Prendere degli avvisi&quot;</td>
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<td>1</td>
<td>4</td>
<td>Procedure ID, worklist evaluation</td>
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<tr>
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<td></td>
<td>Patient identification (bracelet) before the access at pick-up room</td>
<td>Lack of communication</td>
<td>Procedural delay</td>
<td>P.12.732 &quot;Prendere degli avvisi&quot;</td>
<td>2</td>
<td>2</td>
<td>1</td>
<td>4</td>
<td>Revision of procedure, a label to be taken in case of program changes</td>
</tr>
<tr>
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<td></td>
<td>System identification of the patient before the pick-up execution</td>
<td>Procedural error</td>
<td>P.12.732 &quot;Prendere degli avvisi&quot;</td>
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<td>1</td>
<td>2</td>
<td>Revision of procedure, a label to be taken in case of program changes</td>
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<tr>
<td></td>
<td></td>
<td>Identification of culture dishes and storage position inside the incubators</td>
<td>Difficulty in setting on the plates</td>
<td>Procedural delay</td>
<td>P.14.732 &quot;FMIET ICISI Biologia*&quot;</td>
<td>2</td>
<td>2</td>
<td>1</td>
<td>4</td>
<td>Revision of procedure, a label to be taken in case of program changes</td>
</tr>
<tr>
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<td></td>
<td>Incorrect positioning of the dishes inside the incubator</td>
<td>Distraction / work overload</td>
<td>Procedural delay</td>
<td>P.14.732 &quot;FMIET ICISI Biologia*&quot;</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td>2</td>
<td>Revision of procedure, a label to be taken in case of program changes</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Failure to verify the absence of tubes at the end of the pick-up</td>
<td>Procedural error / lack of double check</td>
<td>Partial loss of the material</td>
<td>P.14.732 &quot;FMIET ICISI Biologia*&quot;</td>
<td>3</td>
<td>1</td>
<td>2</td>
<td>6</td>
<td>Revision of procedure, thermolock labeling with identification tag</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Failure to verify the presence of tubes before pick-up execution (double fault)</td>
<td>Procedural error / lack of double check</td>
<td>Google exchange</td>
<td>P.14.732 &quot;FMIET ICISI Biologia*&quot;</td>
<td>5</td>
<td>1</td>
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<td>25</td>
<td>Revision of procedure, thermolock labeling with identification tag</td>
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<tr>
<td></td>
<td></td>
<td>Exchange of culture plates</td>
<td>Procedural error / lack of double check</td>
<td>Loss of oocytes / zygotes</td>
<td>P.14.732 &quot;FMIET ICISI Biologia*&quot;</td>
<td>4</td>
<td>2</td>
<td>1</td>
<td>5</td>
<td>Revision of procedure, addition of the first letter of the patient name in the test report</td>
</tr>
<tr>
<td>2. Sperm collection</td>
<td>Registration and identification of the patient for semen collection, preparation of the sperm for semen collection with attached identification tag</td>
<td>Incorrect data transcription</td>
<td>Distraction</td>
<td>Procedural delay</td>
<td>P.10 &quot;Prendere dati e acquisizione di effetti&quot;</td>
<td>2</td>
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<td>1</td>
<td>4</td>
<td>Procedure ID, worklist evaluation</td>
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<td></td>
<td>Wrong seminal fluid container labeling</td>
<td>Distraction / work overload</td>
<td>Procedural delay</td>
<td>P.10 &quot;Prendere dati e acquisizione di effetti&quot;</td>
<td>2</td>
<td>2</td>
<td>1</td>
<td>4</td>
<td>Procedure ID, worklist evaluation</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Failure or partial control of the correspondence between patient, self-certification and seminal fluid container</td>
<td>Procedural error</td>
<td>Procedural delay</td>
<td>P.10 &quot;Prendere dati e acquisizione di effetti&quot;</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td>2</td>
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<tr>
<td>3. Gamete processing</td>
<td>Transfer of the seminal fluid from the recipient to the tube with the &quot;Identification tag&quot;</td>
<td>Transfer of sperm in the wrong tube</td>
<td>Procedural error / lack of double check</td>
<td>Loss of spermatological zygotes</td>
<td>P.14.732.03 &quot;Creazione e accoppiamento del fertilizzo&quot;</td>
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<td></td>
<td></td>
<td>Corrected decoding, maturity classification and use</td>
<td>Exchange of culture plates</td>
<td>Procedural error / lack of double check</td>
<td>P.14.732 &quot;FMIET ICISI Biologia*&quot;</td>
<td>4</td>
<td>1</td>
<td>1</td>
<td>4</td>
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<tr>
<td>4. Insemination</td>
<td>Identification of the right correspondence between oocytes and must at the moment of insemination</td>
<td>Failure to identify the correct association</td>
<td>Procedural error / lack of double check</td>
<td>Loss of gametes / zygotes</td>
<td>P.14.732.03 &quot;Creazione e accoppiamento del fertilizzo&quot;</td>
<td>4</td>
<td>2</td>
<td>1</td>
<td>8</td>
<td>Revision of procedure, adding label with male partner ID</td>
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<td></td>
<td></td>
<td>Identification of culture dishes and storage position inside the incubators</td>
<td>Distraction</td>
<td>Procedural delay</td>
<td>P.14.732 &quot;FMIET ICISI Biologia*&quot;</td>
<td>2</td>
<td>2</td>
<td>1</td>
<td>4</td>
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<tr>
<td>5. Embryo culture</td>
<td>Association between embryos, culture dishes and storage position inside the incubators</td>
<td>Imperfect transcription of the data on the plates</td>
<td>Distraction</td>
<td>Procedural delay</td>
<td>P.14.732 &quot;FMIET ICISI Biologia*&quot;</td>
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<td></td>
<td></td>
<td>Exchange of culture plates</td>
<td>Procedural error / lack of double check</td>
<td>Loss of embryos</td>
<td>P.14.732 &quot;FMIET ICISI Biologia*&quot;</td>
<td>4</td>
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</tbody>
</table>

*FMS: Failure Mode and Effect Analysis*
Continue from Table 1

<table>
<thead>
<tr>
<th>Patient registration and identification, medical chart updates, and recovery</th>
<th>Inadequate completion of personal data (identification tag and bracelet)</th>
<th>Distraction / work overload</th>
<th>Procedural delay</th>
<th>P.137.32 “Transferimento degli embrioni”</th>
<th>2</th>
<th>2</th>
<th>1</th>
<th>4</th>
<th>POS: standard operative procedures</th>
<th>2</th>
<th>1</th>
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</thead>
<tbody>
<tr>
<td>Patient identification (bracelet) before the access at pick-up room</td>
<td>Not registered patient</td>
<td>Lack of communication</td>
<td>Procedural delay</td>
<td>P.137.32 “Transferimento degli embrioni”</td>
<td>2</td>
<td>2</td>
<td>1</td>
<td>4</td>
<td>Revision of procedure actions to be taken in case of program changes</td>
<td>2</td>
<td>1</td>
<td>1</td>
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<tr>
<td>6. Embryo Transfer</td>
<td>Association between transfer, embryos, transfer culture dishes, and storage position in storage incubator</td>
<td>Inadequate association between the dishes</td>
<td>Procedural error</td>
<td>P.14, 732.03 “Comitato ID della quantità di genitori e degli embrioni durante la gestione biologica”</td>
<td>6</td>
<td>1</td>
<td>2</td>
<td>10</td>
<td>Revision of operating instructions: specifications of the procedure</td>
<td>5</td>
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<tr>
<td></td>
<td>Inadequate association between the dishes and the positions inside the incubator</td>
<td>Distraction / work overload</td>
<td>Procedural delay</td>
<td>P.14, 732.03 “Comitato ID della quantità di genitori e degli embrioni durante la gestione biologica”</td>
<td>2</td>
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<td></td>
<td>Patient identification during embryo transfer in the laboratory (daily scheduled program and biological record)</td>
<td>Inadequate identification</td>
<td>Procedural error</td>
<td>Embryo exchange / mix-up</td>
<td>P.13.732 “Transferamento degli embrioni”</td>
<td>6</td>
<td>1</td>
<td>2</td>
<td>10</td>
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<tr>
<td></td>
<td>Identification of the correspondence between gametes/embryos and cryopreservation device</td>
<td>Inadequate association</td>
<td>Procedural error</td>
<td>Gametes / Embryo exchange / mix-up</td>
<td>P.14, 732.03 “Comitato ID della quantità di genitori e degli embrioni durante la gestione biologica”</td>
<td>6</td>
<td>1</td>
<td>5</td>
<td>25</td>
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<tr>
<td></td>
<td>ID incomplete transcription</td>
<td>Distraction / work overload</td>
<td>Procedural delay</td>
<td>P.06, 732.03 “Ordinamento di genitori e degli embrioni”</td>
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<td>1</td>
<td>4</td>
<td>Workload evaluation</td>
<td>2</td>
<td>1</td>
<td>2</td>
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<tr>
<td></td>
<td>Lack of ID transcription</td>
<td>Procedural error</td>
<td>Line of gametes/embryos</td>
<td>P.06, 732.03 “Ordinamento di genitori e degli embrioni”</td>
<td>4</td>
<td>1</td>
<td>1</td>
<td>4</td>
<td></td>
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<tr>
<td></td>
<td>Identification of the correspondence between cryopreserved material and storage position</td>
<td>Inadequate identification or lack of position</td>
<td>Procedural error</td>
<td>Line of gametes / embryos</td>
<td>P.06, 732.03 “Ordinamento di genitori e degli embrioni”</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td>2</td>
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<tr>
<td>7. Cryopreservation</td>
<td>Recording biological data</td>
<td>Inadequate identification or incomplete data recording</td>
<td>Distraction / work overload</td>
<td>Procedural delay</td>
<td>P.06, 732.03 “Ordinamento di genitori e degli embrioni”</td>
<td>2</td>
<td>2</td>
<td>1</td>
<td>4</td>
<td>Workload evaluation</td>
<td>2</td>
<td>1</td>
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<tr>
<td></td>
<td>Identification of the subject of embryo responsible for the transport</td>
<td>Incorrect / incomplete association between patient couples, recording and sample</td>
<td>Procedural error</td>
<td>Procedural delay</td>
<td>P.21, 732.03 “Transferimento dei tessuti biologicamente immortali”</td>
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</table>
| RPN: risk priority number
The FMEA is a logic analysis, however the failure probability can only be estimated or reduced by understanding the failure mechanism.

In IVF cycles, mix up and gametes or embryos exchange is the worst adverse event that could happen. So embryologists have to improve all the possible strategies to avoid this possibility. In our analysis, the most vulnerable processes are gamete collection execution (pick up) without a correct check and identification of the correspondence between gametes/embryos and cryopreservation device.

For the first process (gamete collection execution) the team suggest a revision of the procedure to reduce the RPN, while for the second process there is no possibility to reduce the risk of failure.

The IVF team recognizes that the possible causes of failures are mainly associated with heavy clinical workload and distraction, communication failures between the team and inadequacy of the labelling system used.

All this causes are typical “human error”, so the possibility of “zero error” is difficult to accomplish, due to conscious automaticity, involuntary automaticity, ambiguous accountability and stress (8).

Rienzi et al. (1) conclude that due to the irreversible and dramatic consequences of mismatches in IVF, it is suggested that safety can be enhanced by performing proactive risk-assessment analysis and by considering the implementation of electronic witness system (IVF Witness, RI, UK) to prevent potential risks.

On this basis our study (that is a part of a multicenter and multidisciplinary Italian study leaded by Italian National Transplant Center, CNT Superior Institute of Health, Rome) confirm the importance of the FMEA analysis and its critical role in IVF program to implement safe for patients, gametes, embryos, prevent errors and develop the involvement to all the personnel of the Unit, considering the importance of the continuous surveillance and review of standard operating procedures and protocols.

References
2. Revised Guidelines for good practice in IVF laboratories 2015.