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Prospective risk analysis adjusted to the reality of clinical and fertility laboratory processes

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Abstract

Background: Prospective risk analysis (PRA) is a valuable instrument in quality assurance. The practical application of PRA in clinical laboratories according to the method we have described elsewhere leaves room for a number of adaptations to make it more applicable to and consistent with actual laboratory processes.
Methods: We distinguished between more and less critical tests and products in the laboratory processes and scored the consequences of failures at different steps in line with the previously described failure type and effect analysis (FMEA) method. PRA was carried out for two typical laboratory processes: standard clinical laboratory testing and the cryopreservation of semen.
Results: Tests in standard clinical laboratory in processes were labeled critical, semi-critical or non-critical. Consequence scoring (C) and assessed risk (R) were significantly higher for processes containing tests considered to be critical (C=6.6±1.5, R=19.3±13.5) as compared to processes containing tests considered semi- or non-critical (C=3.0±1.4, R=8.2±5.3 and C=3.2±1.8, R=8.6±5.9, respectively). There were no differences in the C and R scores for processes with tests considered semi- or non-critical. In the semen cryopreservation process, a distinction between the processes involving private semen and generally accessible semen was made. The C scores for these were significantly different (C=5.9±2.2 and 5.0±2.0, respectively), the R scores did not differ.
Conclusions: Introduction of a test criticality classification for the purpose of consequence scoring led to an improved PRA methodology, better reflecting the reality of clinical laboratory practice. We found that two levels of criticality, critical and less critical, were sufficient to achieve this improvement.

Keywords: clinical laboratory; cryopreservation of semen; failure mode and effect analysis; fertility laboratory; ISO 15189; laboratory testing; process; prospective risk analysis; risk management; semen bank.

Introduction

Modern directives for clinical laboratories require prospective risk analysis (PRA) to be performed for major and critical laboratory processes, in order to identify potential failure points and allow preventive action to be taken [1–3]. The ISO 15189 directive states that ‘the laboratory should take determined action to eliminate potential nonconformities in order to prevent their occurrence’ (paragraph 4.10) and that ‘the laboratory shall evaluate the impact of work processes and potential failures on examination results as they affect patient safety, and shall modify processes the reduce or eliminate the identified risks and document decisions and actions taken’ (paraghraph 4.13.6) [3]. Furthermore, the ISO/TS 22367 (2008) directive states that potential errors and laboratory nonconformities should be identified through the ‘planned review of processes’ [4]. Identifying and eliminating nonconformities to reduce or eliminate identified risks involves PRA and risk management, both of which need to be applied systematically and recurrently to laboratory work processes. According to the ISO/TS 22367 directive, the PRA can be performed

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using a failure mode and effect analysis (FMEA), or any method that identifies the potential for errors, problems or safety risks to patients (paragraph 8) [4].

FMEA involves dividing organizational processes into distinct steps. Within each step, the modes of potential failure are then identified and scored on a digital scale in terms of their probability (P), consequence (C) and chance of detection (D). Multiplication of P and C provides an overall risk score (R) of potential failures per step, which, together with D, is evaluated against predefined criteria. This assessment identifies steps where measures have to be taken to prevent or mitigate the effects of failures [5–10], known as (prospective) risk management [7–11].

For clinical laboratories, PRA is a relatively new activity [12–16]. We have previously published on the topic of FMEA-based PRAs applicable to fertility laboratories, semen banks and clinical laboratories [15, 16]. In our most recent paper we illustrated the use of predefined failure types and convenient matrix tables for scoring [16]. To date, we have applied PRA to eight processes within our department. This brought to our attention a number of anomalies typical for PRAs performed on laboratory processes. One of these observations was that not all 'analytes' or 'products' dealt with in the processes considered are of equal and comparable significance to the users of our services. This drove us to adapt our original PRA method to allow tests and products in specific processes in clinical and fertility laboratories to be distinguished in view of their use and significance for users. In this paper we describe an improved PRA approach as applied to two characteristic laboratory processes: standard clinical laboratory testing and the processing and cryopreservation of semen.

Methods

General approach

PRA was carried out according to the method described previously [16], with some modifications as outlined below. In short, we first drew up an overview of the process being considered in a flow sheet consisting of various steps. A limited set of potential failures was then defined and used in evaluating the different steps. Within this framework, relevant failure points were scored for C and P on a scale of 0–10, and for D on a scale of 1–3 (low – high).

The consequences of potential failures were evaluated with respect to their possible harm to patients. For the standard clinical analytic process, the predefined failure types included 'identification error', 'mixup or loss of material', 'incorrect sample handling', 'incorrect execution of analysis', 'delayed execution' and 'incorrect reporting' (these differ slightly from the failure types defined previously [16]). For the PRA of the processing and cryopreservation of semen, the failure types 'incorrect execution of analysis' and 'incorrect reporting' were replaced by 'incorrect sample treatment' and 'incorrect delivery', respectively. Furthermore, the failure type 'chemical or microbiological contamination' was added, as this is often relevant for gamete processing and is specifically considered in current directives regulating the processing of gametes [17].

The chance of detection was defined as the probability of discovering a failure during the process, i.e. before the reporting of analytical results or the delivery of products, supposing prevention of the failure was possible and implying that external users would not have been aware of it [15]. The realization that a failure is about to occur within a process step being carried out was considered a direct interaction with the operation and was therefore not scored under detection.

During the PRA sessions, P and D were scored per process step simultaneously with C for the process involving more or less critical tests or products. That is for scoring P and D no distinction was made with respect to the criticality of the test or material being processed. This approach was based on the assumption that failures occur in steps, irrespective of the significance of the tests or material being dealt with. The failure types within steps were thus assigned the same P and D scores irrespective of being rated as critical, semi-critical or non-critical issues. Only the scoring of C varied, depending on the significance of the material or test under consideration. Scores were recorded in the columns of the PRA matrix table [16], with the present modification requiring only the addition of one or more columns for the scoring of different C categories. The scores were evaluated as described previously [16], i.e. by classifying the results into the categories 'acceptable', 'suboptimal' and 'in serious need of improvement'.

All of this study was according to national requirements. As neither research was done on animals or patients, nor animal or patient data were involved approval by the Institutional Ethical Board was not required.

Results

Standard clinical laboratory testing

Table 1, part A shows the PRA results for the process of standard clinical laboratory testing, carried out as described previously [16]. In this version of the PRA, which we refer to here as a 'non-discriminating PRA', the process is viewed as a whole; that is, it does not take into account differences in the significance of various tests in terms of clinical diagnosis and decision-making. In contrast, Table 1 part B shows the results of what we call the 'discriminating PRA', where potential failures were scored taking into account the relative clinical significance of the tests. This was carried out by first classifying various laboratory tests into decisive (critical), semi-decisive (semi-critical) and non-decisive (non-critical) for the purpose of clinical decision-making (Table 2). While these distinctions are somewhat arbitrary and dependent on the characteristics and clinical condition of the patient, the list in Table 2 can serve as an aid in scoring the consequences (C) of certain failures in the three abovementioned categories,

Table 1: Overview of the scoring results for different failure types in the PRA for standard clinical laboratory testing.

	Identification error		Mixing up or loss of material		Incorrect sample handling		Incorrect execution of analysis		Delayed execution		Incorrect reporting	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
A. PRA not discriminating beween critical, semi-critical and non-critical test ('non-discriminating PRA')												
Probability (P)	2.2	1.0	2.8	1.1	2.0	1.4	2.0	1.2	4.0	2.5	2.2	1.5
Consequence (C)	6.2	2.0	3.4	1.3	5.0	0.0	6.0	0.0	4.1	1.1	3.8	1.8
Overall risk (R)	13.5	8.3	10.2	6.0	10.0	7.1	12.0	6.9	17.2	13.4	8.2	5.5
Chance of detection (D)	1.8	1.0	3.0	0.0	3.0	0.0	1.8	0.5	2.7	0.5	1.2	0.4
Number of steps scored	6		5		2		4		14		5	
Number acceptable	2		5		2		2		10		2	
Number suboptimal	4		0		0		2		4		3	
Number in serious need for improvement	0		0		0		0		0		0	
B. PRA discriminating beween critical. semi-critical and non-critical test ('discriminating PRA')												
All types of tests												
Probability (P)	2.2	1.0	2.8	1.1	2.0	1.4	2.0	1.2	4.0	2.5	2.2	1.5
Chance of detection (D)	1.8	1.0	3.0	0.0	3.0	0.0	1.8	0.5	2.7	0.5	1.2	0.4
Critical tests												
Consequence (C)	8.0	0.0	6.2	1.8	5.0	2.8	7.0	0.0	6.3	1.6	6.8	0.4
Overall risk (R)	17.3	7.9	16.4	6.5	12.0	12.7	14.0	8.1	25.2	18.1	15.0	10.5
Number of steps scored	6		5		2		4		14		5	
Number acceptable	2		5		2		2		7		2	
Number suboptimal	4		0		0		2		4		3	
Number in serious need for improvement	0		0		0		0		3		0	
Semi-critical tests												
Consequence (C)	7.0	0.0	2.8	0.4	2.5	0.7	3.0	0.0	2.0	0.4	2.8	0.4
Overall risk (R)	15.2	6.9	7.6	2.6	5.5	4.9	6.0	3.5	8.2	6.0	6.0	4.2
Number of steps scored	6		5		2		4		14		5	
Number acceptable	2		5		2		3		11		2	
Number suboptimal	4		0		0		1		3		3	
Number in serious need for improvement	0		0		0		0		0		0	
Non-critical tests												
Consequence (C)	6.0	0.0	2.8	0.4	2.5	0.7	3.0	0.0	2.0	0.4	2.8	0.4
Overall risk (R)	13.0	5.9	7.6	2.6	5.5	4.9	6.0	3.5	8.2	6.0	6.0	4.2
Number of steps scored	6		5		2		4		14		5	
Number acceptable	2		5		2		3		11		2	2
Number suboptimal	4		0		0		1		3		3	
Number in serious need for improvement	0		0		0		0		0		0	

Table 2: Example of how standard clinical laboratory tests might be distinguished in critical, semi- critical and non-critical, in view of their clinical use.

Critical tests	Semi-critical tests	Non-critical tests
Activated partial thrombin time (APTT)	Antithrombin-3	Angiotensin converting enzyme (ACE)
Ammonia	Aspartate aminotransferase	Albumin
Amylase	Alanine aminotransferase	Bilirubin, conjugated
Anti-fXa (anti-coagulation factor Xa)	Alkaline phosphatase	Chloride
Bilirubin (total)	CA 125	Cholesterol
Calcium	Carcino embryonic antigen (CEA)	Folic acid
Chorionic gonadotropin (hCG)	Cell count in body fluids (not blood/urine)	HDL-cholesterol
Cortisol	Creatin kinase	Lactate dehydrogenase
C-reactive protein (CRP)	Eosinophil count	Phosphate
Creatinin	Erythrocyt sedimentation rate (ESR)	Protein (total)
D-dimer	Ferrtin	Protein (urine)
Estradiol	α Fetoprotein	Testosteron
Erythrocyte count	Follicle stimulating hormone (FSH)	Transferrin
Fibrinogen	IgA	25-OH Vitamin D
Glucose	IgG	Vitamin B12
Leukocyte count	IgM	
Leukocyte differentiation	Insulin	
Lipase	Iron	
Lithium	Y-Glutamyl transferase	
NT-proBNP	Luteinising hormone (LH)	
Potassium	Magnesium	
Prolactin	Normoblast count	
Prostate specific antigen (PSA)	Parathyroid hormone (PTH)	
Protein (cerebrospinal fluid)	Progesteron	
Prothrombin time (PT)	(Pseudo)cholinesterase	
Sodium	Reticulocyte count	
f-T4 (free thyroxin)	Triglycerides	
Troponin	Triiodothyronin (T3)	
Thyroid stimulating hormone (TSH)	Urea	
Thrombocyte count	Uric acid	

All tests refer to testing in blood, unless otherwise indicated.

taking into consideration the harm a failure in testing may cause.

The mean scores for R and C of different failure types in the discriminating PRA ranged between 5.5–25.2 and 2.0–8.0, respectively, with the highest values being found for the testing of critical analytes (Table 1, part B). For all six potential failure types, the mean R and C scores were higher for critical tests than for semi- and non-critical tests. The highest mean R score (25.2) was obtained for critical tests of failure type 'delayed execution', which was mainly due to the probability of this type of failure scoring the highest of all failure types (mean P=4.0). In the non-discriminating PRA this was also the failure type with the highest R score (17.2), for similar reasons (Table 1, part A). This indicates that on-time delivery is considered one of the most vulnerable aspects of our laboratory processes. The failure type 'identification error' scored second highest for critical tests in the discriminating PRA (mean R=17.3), mainly due to receiving the highest score for C (mean C=8.0). In the non-discriminating PRA, this failure also obtained the second-highest R score (mean R=13.5) for the same reason (mean C=6.2).

In the discriminating PRA, 38 failure points were rated suboptimal or in serious need of improvement. For processes involving critical tests, 13 were rated suboptimal and three in serious need of improvement, while for those involving semi- and non-critical tests 11 were rated suboptimal in each category (Table 1). In the non-discriminating PRA a total of 13 failure points were rated as suboptimal, while no failure points were deemed to be in serious need of improvement. Combining the results of the critical, semi-critical and non-critical testing classes, the discriminating PRA identified 'delayed execution' as the failure type most often rated suboptimal (10 times) or in serious need of improvement (three times). Most of the suboptimal failure points (4) and all three in serious need of improvement were identified in the process involving critical tests. The second highest rated failure type detected

by the discriminating PRA was 'identification error' (12), although in this case no difference was detected in the R scores for processes involving critical, semi-critical and non-critical tests (4 for each).

For the two failure types 'mixup or loss of material' and 'incorrect processing or handling', no suboptimal R scores were observed. High R scores were found for these three failure points in the non-discriminating PRA, although these were lower than those observed in the discriminating PRA. This lower scoring was a result of the consequences being scored lower in the non-discriminating PRA versus the discriminating PRA (5 vs. 6 or 7, respectively).

A more detailed PRA was carried out for the three failure points rated in serious need of improvement and measures were taken to reduce the chances of these failures taking place.

Cryopreservation of semen

Similar to the standard clinical lab testing PRA methodology, we also introduced a criticality classification in the PRA procedure for semen cryopreservation. Taking the significance of the processed material into account, we distinguished 'private semen' from 'generally accessible semen'. Private semen came from private donors and from men who were preserving their own semen (e.g. prior to cancer treatment). In analogy to the distinctions made in standard clinical lab testing, this private material may be considered 'critical'. Generally accessible semen was defined as semen from independent anonymous donors, which can be used by a number of women with no personal connection to the donors or the cryopreserved material. This type of semen and its processing may be considered 'less critical'. The processes outlined for the cryopreservation of private semen and generally accessible semen were very similar, though not identical, given that some failure types are not relevant for private material, such as checking and controlling the number of pregnancies resulting from a specific donor or reserving specific donor semen for particular recipients (e.g. once a woman becomes pregnant and would like to have another child by the same donor). Given the significant differences between private and generally accessible semen, we did not carry out a non-discriminating PRA for the process of semen cryopreservation, but instead proceeded immediately with the discriminating PRA methodology.

For the process of semen cryopreservation, a total of 32 steps were outlined, within which 143 potential failures were scored for seven predefined failure types (Table 3). The PRA results for generally accessible semen included five failure points that did not arise in the PRA results for private semen. As a result, fewer potential failures were identified in the process involving private material (66) as compared to that of generally accessible material (77).

The mean R and C scores of different failure types ranged between 4.5–16.2 and 2.0–7.0, respectively (Table 3). In the process involving private semen, the highest mean R and C scores were observed for five and four specific failure types, respectively. In the process involving generally accessible semen, the R and C scores were highest for two and three failure types, respectively. For two specific failure types, the PRA for generally accessible semen recorded higher mean C and R scores than the PRA for private semen. This was due to the presence of several failure points (with relatively high scores) in the cryopreservation process for generally accessible semen, which were not present in the process for private semen. In the case of failure type 'chemical or microbiological contamination' R and C were scored lower for private material than for generally accessible material, given that the impact of the former was considered lower.

The highest mean R score was observed for the process of private semen cryopreservation under failure type 'incorrect sample treatment' (16.2). This occurred due to the high score for C (mean=6.9), but also as a result of P (mean=2.4) scoring the highest of all failure types. The failure type 'loss of material or wrong sampling' scored second highest (mean R=13.0), due to the relatively high scores for both P (mean=2.0) and C (mean=6.6). Furthermore, the failure types 'identification error' and 'incorrect sample treatment' received the highest mean C scores (7.0 and 6.9, respectively) in the process of private semen cryopreservation. In the generally accessible semen cryopreservation process, the highest mean R score was observed for 'identification error' (10.8).

In total, 29 failure points were rated suboptimal in the PRA of semen cryopreservation: 14 in the process involving private semen and 15 in that of generally accessible semen (Table 3). No process steps were evaluated to be in serious need of improvement. Overall, 'identification error' was most often rated as suboptimal (12 times): five times in the process for private semen and seven times in that for generally accessible semen cryopreservation. This difference resulted from the fact that pregnancy scoring plays no role in the process involving private semen and that the consequence of microbiological testing was rated lower for private semen. Otherwise, the numbers of failure points classed as suboptimal were comparable for the different failure types. Notably, no failure points were evaluated as suboptimal for the failure type 'delayed processing'.

Table 3: Overview of the scoring results for different failure types in the PRA for cryopreservation of semen.

	Identification error		Mixing up or loss of material		Incorrect sample handling		Chemical or biologic contamination		Incorrect sample treatment		Delayed execution		Incorrect delivery	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Private semen														
Probability (P)	1.6	0.7	2.0	0.8	2.0	1.0	1.3	1.5	2.3	1.1	2.5	0.7	1.5	0.8
Consequence (C)	7.0	1.4	6.6	2.0	4.7	3.1	3.3	0.7	6.9	1.8	2.0	0.0	4.8	2.0
Overall risk (R)	11.0	5.5	13.0	6.5	10.7	11.5	4.5	5.8	16.2	8.4	5.0	1.4	6.3	2.0
Chance of detection (D)	2.5	0.8	2.7	0.6	2.0	1.0	1.0	0.0	2.6	0.7	3.0	0.0	2.5	0.8
Number of steps scored	25			11	3		8		9		2		8	
Number acceptable	20			10	2		5		6		2		7	
Number suboptimal	5			1	1		3		3		0		1	
Number in serious need for improvement	0			0	0		0		0		0		0	
Generally applicable semen														
Probability (P)	1.7	0.8	2.0	0.7	2.0	1.0	1.3	1.5	2.3	1.1	2.0	0.8	1.6	0.7
Consequence (C)	6.4	1.3	3.1	1.7	4.0	2.0	5.0	0.0	4.1	1.9	2.8	1.5	5.6	2.2
Overall risk (R)	10.8	5.5	6.5	4.8	6.7	1.2	6.3	7.4	9.4	6.9	4.8	1.0	7.8	3.0
Chance of detection (D)	2.4	0.9	2.8	0.6	2.0	1.0	1.0	0.0	2.7	0.7	3.0	0.0	2.3	0.9
Number of steps scored	29			12	3		8		12		4		9	
Number acceptable	22			11	2		5		11		4		7	
Number suboptimal	7			1	1		3		1		0		2	
Number in serious need for improvement	0			0	0		0		0		0		0	

For the four failure points evaluated as suboptimal, a more detailed analysis was subsequently carried out and improvements were considered.

Overview of all discriminating PRA results

In the discriminating PRA for standard clinical lab testing for which critical, semi-critical and non-critical test classes were distinguished, a total of 16 process steps with 108 potential failures were scored for the six predefined failure types. This were three times more potential failures than in the non-discriminating PRA (Table 4). Mean R and C scores in the discriminating PRA decreased from high to low, down the criticality spectrum (from critical to semi-critical to non-critical tests). The R and C scores of critical and semi-critical tests were significantly different ($p<0.0001$ for both scores; two-sided unpaired t-test). The differences between the R and C scores of semi- and non-critical tests did not reach significance ($p<0.76$ and $p<0.60$, respectively). The overall scores of R and C in the non-discriminating PRA fell between those of the critical and semi-critical tests in the discriminating PRA results (Table 4).

In the PRA for cryopreservation of semen, the mean R and C scores tended to be higher for the processing of private material (R=10.5, C=5.9) than for the processing of generally accessible material (R=8.6, C=5.0) (Table 4). The differences in C were statistically significant ($p<0.01$), while those in R did not reach significance ($p<0.07$).

Discussion

Typically, the processes in clinical laboratories comprise a range of analytes with divergent pathophysiological origins and diagnostic relevance. As a result, failures can have vastly different consequences, depending on the analytes involved. Significant delay, sampling, analytical or reporting errors in the testing of serum glucose, potassium or hemoglobin, for instance, have more serious consequences than similar failures in the testing of serum cholesterol, phosphate and most enzymes. Erroneous or late reporting of abnormal results of the former may result in serious complications. In contrast, failure in reporting of the latter may lead to delayed diagnosis or postponed treatment for non-acute disease, being inconvenient, but not involving increased, serious, risk. Similar variability can be seen in the consequences of failures occurring in the processes of products for fertility treatment (sperm), which in the Netherlands is often coordinated by clinical laboratories. A failure in a process involving private semen (e.g. a young male preserving his semen in advance of cancer treatment) will have a vastly different impact than a failure involving donor semen that is used for multiple prospective parents.

The two processes we considered in the present paper illustrate the variability in identity and (clinical) significance of analytes or products that laboratory processes typically consist of. Other laboratory processes are similarly variable and the quality of the PRA of these

Table 4: Summary of the results of the collective discriminating PRA's.

A. PRA of standard clinical laboratory testing	**Discriminating PRA, distinguishing variable relevance of testing**			**Non-discriminating PRA**
	Critical tests	**Semi-critical tests**	**Non-critical tests**	**Tests viewed all the same**
Mean overall risk, R (±SD)	19.3 (13.5)	8.6 (5.9)	8.2 (5.3)	15.5 (11.7)
Mean consequence, C (±SD)	6.6 (1.5)	3.2 (1.8)	3.0 (1.4)	4.6 (1.6)
Number of steps scored	36	36	36	36
Number acceptable	20	25	25	23
Number suboptimal	13	11	11	13
Number in serious need for improvement	3	0	0	0
B. PRA of cryopreservation of semen	**Private material**	**General material**		
Mean overall risk, R (SD)	10.5 (6.9)	8.6 (5.6)		
Mean consequence, C (±SD)	5.9 (2.2)	5.0 (2.0)		
Number of steps scored	66	77		
Number acceptable	52	62		
Number suboptimal	14	15		
Number in serious need for improvement	0	0		

may improve similarly by distinguishing the significance and application of the tests and products processed. We sincerely belief that considering a process without acknowledging the large variability in significance and applicability of these issues results in a superficial, distorted and unrealistic PRA. As a result, the standard FMEA approach requires adjustment to be appropriate and of optimal use for laboratories. We resolved this issue by integrating into our previously published PRA methodology [16] a distinction between the criticality levels of tests or products. The consequences of potential failures in process steps were scored separately, taking into account how critical the tests or products were. In our opinion, this led to a better and more appropriate PRA result. Irrespective of the criticality of the analyte or product, the chance of failures occurring in the different process steps, and therefore the probability ratings (P), will be the same.

The consequences and overall risks received significantly higher scores for critical issues (test or material) as compared to less critical issues. There was little difference, however, between the C and R scores of tests considered semi- and non-critical. On closer inspection, they differed only for the failure type 'identification error', a distinction in scoring (C rated as 7 or 6) that could be considered arbitrary. In fact, the classification of tests and analytes as either semi- or non-critical (Table 2) is also necessarily subjective. Our team was unable to unanimously rank certain tests as semi- or non-critical for clinical decision-making; for instance, different views existed about the categorisation of tests for aminotransferases, alkaline phosphatase, (pseudo)cholinesterase, uric acid, normoblasts and reticulocytes. This leads us to conclude that that the distinction between semi- and non-critical tests was superfluous. It appears sufficient to distinguish between just two categories in standard clinical laboratory testing: tests critical for clinical decision-making and tests less critical in that respect. Indeed, it is even arguable which tests should be considered critical. Examples may include those tests for which alert values have been defined because the results above certain thresholds are regarded as imminently life threatening [18, 19]. Ultimately, however, exactly which tests are identified as critical is irrelevant; the key is that for optimal results no more than two categories of tests should be distinguished.

In the PRA on the semen cryopreservation process, assigning 'critical' and 'less critical' labels was even more challenging than for laboratory testing. While private semen might be viewed as critical and generally accessible semen as less so, this description does not hold for all aspects of the processes. For some failure types, the impact of failures may be considered greater for generally accessible than for private semen. An example is microbiological and chemical contamination: for insemination between partners lower standards of microbiological safety are accepted than for insemination of women with material from donors unknown to them [17]. The responsibility for preventing the transmission of infection from donor semen lies in the hands of physicians collecting donations and the laboratory processing the products. In contrast, in the case of private semen cryopreservation microbiological transmission can also occur between partners, and so the weight of responsibility is borne by the provider and the recipient of the semen sample. This led to lower scores for C (and R) for private as compared to generally accessible material for the relevant failure points. In addition, the processes involved in private and generally accessible semen cryopreservation are not entirely similar, at least in our laboratory. Process steps related to the registration and control of pregnancies do not apply to private semen donations. Since some of the failure types in these steps obtained high ratings for C, the mean C and R scores in the PRA for private semen cryopreservation were not overtly higher than those for cryopreservation of generally accessible semen.

Carrying out a PRA entails identifying all potential failures and scoring P, C and D. Appropriate scoring is central to the enterprise, but also its most vulnerable element, given the difficulty in defining failures and their possible consequences. In this paper we have presented an improved PRA methodology, with the scoring of consequences tailored to the impact of failures depending on the significance of the issues processed. This was achieved by distinguishing between processes that are considered critical and less critical at the level of analytes or products. In our view, this does justice to the reality of laboratory processes and facilitates more realistic scoring.

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