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Introducing SI-PEA: a Risk-based Tool to Measure the Effectiveness of Your Self-inspection Programme

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Introducing SI-PEA – a risk-based tool to measure the effectiveness of your self-inspection programme

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Abstract

Self-inspection is a requirement of most Quality Management Systems. Within an organisation, it is a key process for self-assessing compliance to regulatory requirements. Done well, it can be a very informative system – highlighting gaps and driving improvement. However, these audits can vary in effectiveness and the contribution of the programme can be difficult to assess and measure. Ensuring that there is an effective system in place is challenging.

This paper assesses how the effectiveness of self-inspection programmes is currently measured and reviews the expectations of quality system regulations and standards. Based on this research, a Self-Inspection Programme Effectiveness Assessment (SI-PEA) tool was developed. SI-PEA is a risk-based method for assessing effectiveness of the self-inspection programme, verifying compliance to current quality system regulations, and identifying if there are opportunities to improve the programme. The tool ultimately assigns a risk score to the programme's overall effectiveness. The tool was developed for application in a pharmaceutical quality system but is suitable for application within any quality management system. The developed SI-PEA tool has been successfully piloted across two companies to prove its functionality.

Introduction

In the European Union (EU), self-inspection is a requirement of a pharmaceutical quality system and is used to monitor the application of Good Manufacturing Practice (GMP) [1] through the Quality Management System (QMS). Specifically, the requirement is that '*There*

is a process for self-inspection and/or quality audit[1], which regularly appraises the effectiveness and applicability of the Pharmaceutical Quality System'

The objective of self-inspection is to monitor the company's compliance with GMP requirements, identify gaps, and implement change as required. The self-inspection programme is also a mechanism to highlight areas of continuous improvement within the QMS. The International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) in their *Q10 Guidance: Pharmaceutical Quality System* [2] recommends using self-inspection as one performance indicator of the effectiveness of a quality system and as a means of identifying innovations that might enhance the quality system. The challenge is to understand how well the programme achieves these objectives.

This research created a method or tool to measure the effectiveness of a self-inspection programme using a *risk-based approach*. This tool both assesses the performance of the self-inspection programme and identifies opportunities for improvement, aligning with the intent of ICH Q10. A risk score is assigned based on the assessment criteria and this score is then used to track improvements to the programme, thereby demonstrating improvement.

There were four stages and methods utilised in this research:

1. A **Literature Review** was performed to summarise the expectations of a self-inspection programme across several quality system standards. This was supplemented with a review of publications specifically discussing the effectiveness of self-inspection

2. A **survey** was conducted with quality specialists within the pharmaceutical industry to understand the current approaches to monitoring and improving self-inspection programmes

3. An **interview** was conducted with a representative of a regulatory authority – and published expert on this topic -to understand expectations

4. The **tool was developed and piloted** across two companies. The output was analysed and determined to be informative and useful.

[1] Throughout the documents reviewed for this paper, the term *self-inspection* is interchangeable with the term *internal au*dit. The meaning of both terms is the same and therefore no differentiation will be made throughout this paper.

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Literature Review

Self-Inspection is a requirement of many quality system standards and regulations. The standards selected for this review apply to the pharmaceutical industry or related sectors, such as the medical device sector. These references were used to develop a matrix of requirements (TABLE 1). The intent in analysing these requirements was to assure that all the requirements were captured in any subsequent assessment process.

It was noted that, while there is a requirement to perform internal audits in the US Food and Drug Administration (FDA) quality system requirements for medical devices 21 CFR 820 [3], there is no requirement in the US pharmaceutical regulation 21 CFR 210/211 [4]. However, FDA have contributed to and endorsed ICH Q10 which, as discussed previously, recommends self-inspection as a key element in QMS performance review. Therefore both 21 CFR 820 and ICH Q10 were reviewed in detail for self-inspection requirements

In addition, FDA are a member of the Pharmaceutical Inspection Co-Operation Scheme (PIC/S). The PIC/S recommendation on QMS requirements for Pharmaceutical Inspectorates [5] advises on the assessment of Internal Audit within a QMS under inspection. Therefore, this was included also.

Key: X = Requirement referenced / Grey = No requirement							
Key Highlighted Requirement	**EudraLex** [1]	**21 CFR 820.22** [3]	**ICH Q10** [2]	**ISO 9001** [6]**/ ISO 13485** [7]	**ISO 19011** [8]	**GVP** [9]	**PIC/S** [5]
Procedure in Place		X	X	X	X	X	X
Details within procedure			X	X	X		X
Risk Based approach to planning (frequency)			X	X	X	X	X
Risk factors defined			X	X	X	X	
Auditor competency	X	X	X	X	X	X	X
Auditor competency details					X	X	X[2]
Records of Findings	X	X	X	X	X	X	X
Use of CAPAs	X	X	X	X	X	X	X
Incorporated root cause and impact analysis						X	
Records review by Management	X	X	X	X	X	X	X
Specific reference to audit area management				X	X	X	
Re-audit		X			X	X	
Audit programme evaluation					X	X	

Table 1: Summary of Review of Regulations, Standards & Guidance

The quality standards of the International Standards Organisation (ISO) were also included in the review. The review included both the current version of the general quality standard, *ISO 9001:2015 Quality Management Systems* [6] and the specific requirements for the Medical Device industry – ISO 13485:2016 [7]. The ISO suite of standards also has a specific standard for the application of internal audit – *ISO 19011:2018 Guidelines for Auditing Management Systems* [8]. This standard details expectations in relation to internal audit and is referenced in the PIC/s document previously mentioned and was, therefore, included in this review.

Both the EU GMP Requirements – Eudralex Volume 4 [1] (specifically Chapters 1 and 9) as well as those documented in the Good Vigilance Guidance [9] were included. Although GVP guidances do not form part of the EU GMP requirements, they contain much more detailed recommendations on self-inspections and therefore were included in this review.

[2] Cross Reference to ISO 19011

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The outcome of this analysis is summarised in TABLE 1. The comparison established, that although there are many common requirements, there are some differences in expectations and also in the level of detail.

For example, the use of a risk-based approach to the determination of frequency and duration of self-inspection is not mentioned in either of the regulations included in the review – Eudralex Volume 4 or 21 CFR 820. However, it is mentioned in the guidance and standards reviewed. The usefulness of the risk-based approach has, however, been mentioned in presentations by competent authorities [10] and may be regarded as a current expectation of the process. By identifying those areas within the operation that are most complex or that have indicated negative trends within the QMS e.g., monitoring of issues, change or competence – the programme can more effectively apply its resources. This is an approach taken by the authorities themselves when assessing audit frequency and duration of facilities [11]. It is therefore included as an expected application in this work. In addition to using a risk based approach for determining frequency and duration, Jeroncic [12] describes the use of risk based approach as part of planning and conducting of self-inspection to ensure their effectiveness.

Another interesting example of inconsistency is the requirement for auditor impartiality and competency. While this is a requirement described in both EudraLex Volume 4 and 21 CFR 820.22, there are no further details outlined. ISO 19011:2018 does detail these requirements and this standard is cross- referenced in the PIC/s QMS requirements for Pharmaceutical Inspectorates. This indirect reference implies that is an expectation. The matrix of expectations was used to inform the developed tool. However, to assist in resolving some of these inconsistencies in expectations, the interview with a regulatory authority representative was included in the process.

In an interview with a regulatory authority senior GMP Inspector, O'Donnell [13] highlights some areas within a self-inspection program that should be critically examined in order to increase value of their self-inspection program thereby improving effectiveness. One of the areas described is that the inspections are carried out in the right areas, in the right intervals, and by the right personnel. Such criterion have also been identified throughout the analysis as per TABLE 1 as well as being incorporated into the SI-PEA tool.

Further literature review focused on the measurement of effectivity of the self-inspection system. There were some informative contributions. Hanim Fraudziah et al [14] described measuring the effectiveness of self-inspection based on a review of the self-inspection procedures and assessing compliance with the applicable standards. However, these authors considered that this approach represents an audit of the *compliance* of the audit process and does not constitute a measure of its *effectiveness*.

Dittenhofer [15] approached measuring effectiveness by reviewing audit outcomes. An audit programme was considered effective when there were no findings or when findings were resolved. This approach is common in the pharmaceutical industry as evidenced by a survey conducted as part of this research. However, the flaw with this approach is the inability to determine whether a lack of audit findings is due to satisfactory implementation of the QMS or an incompetence of the self-inspection programme with respect to identifying deficiencies. This research concluded that this approach alone was not an adequate assurance of effective application of the programme.

To further develop this review, the work of O'Mahony [16] was studied in detail. O'Mahony analysed the findings of one regulatory authority – the HPRA (Health Products Regulatory Authority of Ireland) with respect to self-inspection deficiencies identified in inspections from 2013-2017 (Table 2). Note this does not reflect all inspection types performed by the HPRA.

Deficiency Type	# times cited
Lack of/ Inadequate Procedure	14
Failure to apply Quality Risk Management	14
Lack of Management Commitment	11
Audit Resources/ Training	11
Schedule Adherence	11
CAPA implementation and closure	8

Table 2: Summary of HPRA Self-Inspection Findings 2013-2017

Of interest from this study is that compliance with the requirements, as suggested by Hanim Fraudziah, is a performance factor that cannot be excluded from an assessment of the programme, as it represents the most common deficiency. However, this may also be due to a lack of clarity on the details of expectations in this area. O'Mahony concluded in her work, that further clarity in the regulations would improve the application of the programme.

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It was further noted that failure to apply a risk-based approach to the programme was also a common deficiency. This assured these authors that including the requirements of related guidance's and recommendations was appropriate to assure that *current* expectations of the programme were part of the evaluation of its performance.

Expert Interview

The author of the previously referenced work, Denise O'Mahony, is a Pharmaceutical Assessor at the HPRA. This interviewee was chosen based on her current role, her experience working in a regulatory authority, and her own research work on the topic through her M.Sc. dissertation titled *'GMP Chapter 9 Self Inspection Programme'* [16] and related presentations [17]. It is important to note, however, that the views expressed were personal reflections based on research and, while offering a perspective from outside industry, the views expressed did not represent those of the HPRA and should not be concluded as such.

The interview was conducted through email. The questions were based on the research work of the interviewee and were designed to inform the proposed tool. When asked about key identifiers of effectiveness for a self-inspection programme the interviewee highlighted the importance of both overall programme structure and management commitment, while noting the challenge in effectively measuring the latter. This was considered when designing the assessment tool and an assessment of management involvement was included.

The interviewee was also asked for her views on the potential usefulness of an assessment tool and if it would be of benefit in a regulatory inspection. She expressed a view that an appropriate tool could be used to demonstrate the effectiveness of Self Inspection within the PQS. She noted the importance of being able to demonstrate the effectiveness of the pharmaceutical quality system, a key requirement in availing of any regulatory relief. This is an opinion echoed by her HPRA colleague - O'Donnell [10] who has stated that, *'A key to (regulatory) relief is demonstrating the effectiveness of the Pharmaceutical Quality System, as outlined in the ICH Q10 annex'.* Consequently, the proposed tool uses a risk-based approach and incorporates the principles of ICH Q9: *Quality Risk Management* [18] and Q10.

The interviewee was also asked her opinion on whether informal tools or independent checks, such as walkabouts, mini audits, or checklists, might be useful to supplement the formal audits of a self-inspection programme. The interviewee did not have a definitive view and highlighted that this could depend on the process in question. To this point, the industry survey as described in the next section, showed 40% of respondents using a combination of tools as part of their self-inspection programme. These tools were considered particularly effective at identifying opportunities for improvement. Continuous improvement is an important element when demonstrating the effectiveness of the overall QMS.

Industry Research – Survey

To understand how self-inspection programmes are currently monitored and determined to be effective, a research survey was conducted using a '*Self-Inspection Programme Effectiveness Questionnaire'*. The survey consisted of 15 questions, designed to inform the development of a risk-based measurement tool.

The form consisted of three sections; The first section was designed to establish the demographic of the responders, establish the industry sector in which they worked, and the role they had within the organisation. The second section was aimed at understanding the responder's general opinion towards a self-inspection programme. The third section attempted to clarify the respondents own self-inspection programmes and process.

Section 1 – REPONSE DEMOGRAPHIC

Due to COVID-19 restrictions, Microsoft Forms was used to conduct the survey. The link was shared through LinkedIn and by direct email. Therefore, it is difficult to evaluate the number of respondents invited to contribute with the number of responses received. In total, 25 respondents completed the survey within 30 days of release. All respondents completed every question, including the open free text questions.

Most of the respondents worked within the Biopharmaceutical industry (52%), a further 28% within Pharmaceutical, and 8% in the Medical Device sector. Of the 25 user respondents, 15 worked within Quality Assurance and 6 worked in Quality Control. Two of the respondents were heads of site and internal auditors.

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Section 2 – Role of Self Inspection

When asked to rate the value of a self-inspection on a scale of 1-5 (1=low /5=high) responses ranged from 3 to 5, with an average score of 4.4. This indicates that the programme is considered a valued element in the quality management system. Respondents were asked to provide a free text reason for this score and the replies are summarised in Table 3.

No. Responses	Reasoning
8	External audit readiness / GMP compliance
13	Continuous Improvement opportunity / way to highlight problem areas.

Table 3: Reasons why the Self Inspection Programme is valued

It was noted that these reasons were provided by those that assigned a high value score to the programme (4-5). Three respondents assigned a lower score of 3 to the programme, explaining that the self-inspection programme was not applied with the same level of rigidity as external or regulatory audits.

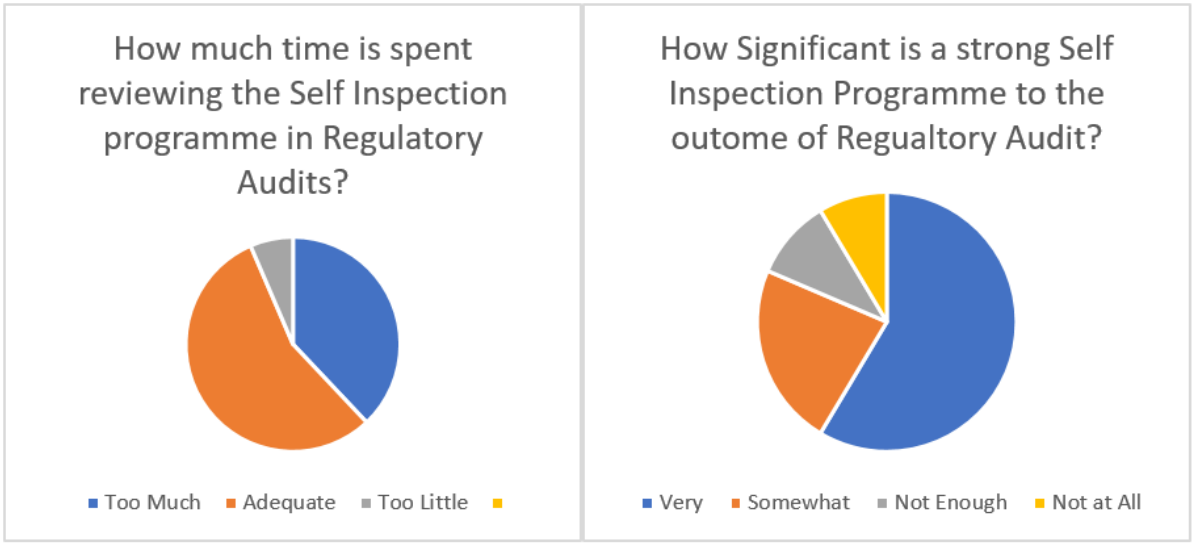


Figure 1: Survey summary responses

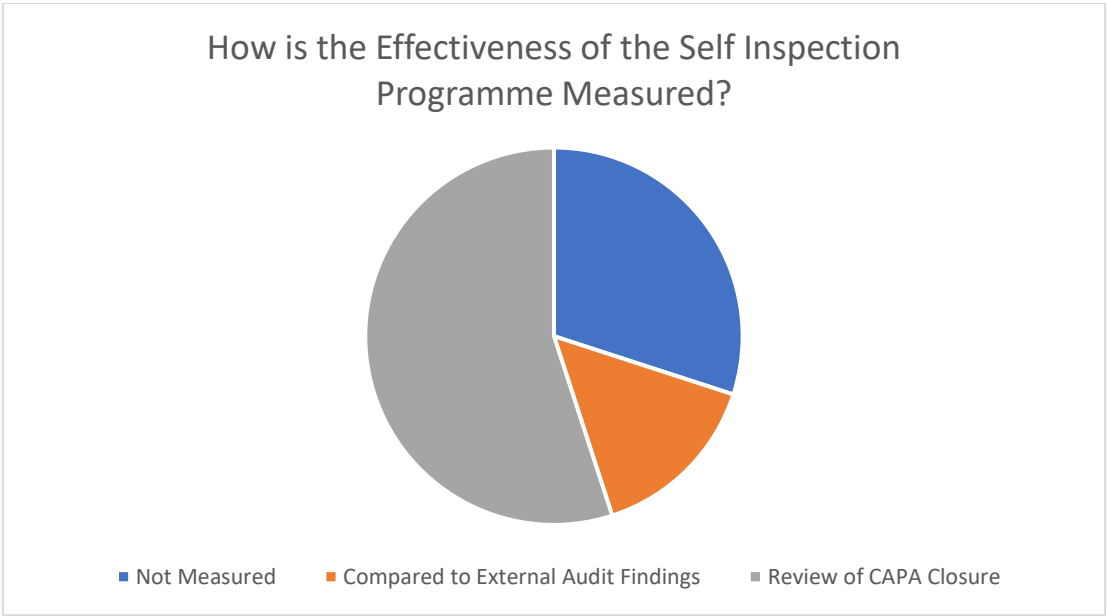
It was clear from the responses that the respondents considered the Self Inspection programme as a valued element of the quality management system and that it was viewed as a key tool for assuring compliance in regulatory audit. Given that it was considered such a valued system, it was therefore interesting to determine how it was monitored by the respondents.

88% of respondents indicated that they apply a categorisation scheme to the findings of Self Inspection. This is consistent with both ICH Q10 and ISO 19011:2018, both of which recommend ranking findings to prioritise findings and aid in determining the scope of the CAPA (Corrective and Preventive Actions) required.

To determine if these internal audits were a robust preparation for a regulatory audit, 64% indicated up to 25% of findings were categorised as major. This indicates that the programme is contributing to the prevention of findings in regulatory audit. However, it reveals little information about the overall effectiveness of the programme or of its role in continuous improvement.

Section 3 – Monitoring Self Inspection

When asked how the effectiveness of their self-inspection programme is measured (free text), 30% indicated that it was not measured. Considering how valued the system was rated, this appeared to be high. Of those that did measure the system, 55% indicated that the evaluation was based on the number of CAPA's raised, their timely closure, and lack of re-occurrence of the issue. When asked, the respondents indicated that these were also the criteria used to evaluate the programme in Management Review[3].



[3] Management Review, a periodic evaluation of the QMS, is also a requirement of many quality standards.

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This is significant to this research as it provided evidence that, despite being a means of monitoring the QMS, the programme itself does not have a comprehensive measurement or monitoring system.

To get full value from the survey, it was decided to add some questions relating to the application of Quality Risk Management (QRM). It was noted in the literature review that this was a concern to regulatory inspectors and, in O' Mahony's work, it was a significant reason for regulatory citations. When asked how the frequency of self-inspections is determined, only 68% responded with 'based on Risk Assessment'. When surveyed for key influences in deciding audit scope, 20% indicated that it is solely based on previous audit history. Based on the responses, it can be deduced that between 20-30% of self-inspection programmes do not include a risk-based approach to determining audit frequency and scope.

Responders were also asked about the level of formality applied to the self-inspection programme and were asked about the use of formal and informal tools. The use of less formal continuous improvement tools e.g., Gemba walks, personnel discussions, or interviews, provide potential to reduce the number of formal audits, as suggested by Duran [19]. 52% responded that only formal audits processes were used, while only 40% indicated that they used a combination of informal tools and formal audits. Further questions determined that of the 13 respondents who reported using formal audits only, 6 of them do, in fact, use additional tools as part of their self-inspection programme, but do not see them as a means of broadening the impact of the programme.

Development of the SI-PEA Tool

Using a template previously developed by Mulholland to apply a risk-based approach to determining the frequency, duration, and scope of self-inspection, the authors applied the outcomes of the above research to develop an assessment tool. It was decided to apply 10 criteria to the assessment, including those criteria already applied within all companies surveyed i.e., adherence to schedule, number of findings, CAPA implementation, and lack of issue re-occurrence.

Based on all the considerations previously mentioned, the authors added the criteria identified when analysing the requirements of the regulations, standards and guidance and the most common reasons for self-inspection deficiencies in regulatory audit– compliance of the programme and the application of QRM. Table 4 indicates the criteria used and the justification for the application of each effectivity measurement criteria.

Figure 2: Self-Inspection Programme Effectiveness Assessment (Makarevich,2020)

Control System:	If Total Rank Score >60, major improvements to internal audit programme are required ● If Total Rank Score >30, deficiencies in the internal audit programme ● If Total Rank Score <30, areas of improvement identified for audit programme effectiveness ●

A ranking system was developed, ranking each criterion with a score from 0 to 5, where 0 indicates good compliance and a low level of risk and 5 indicates potential area of improvement for the self-inspection programme. Makarevich developed an excel spreadsheet and applied a drop-down menu option to prevent values outside of this rank rating from being selected. The overall rank was calculated across all 10 criteria. The lower the score, the greater the performance with the system. The maximum risk score value is 90, indicating a total lack of effectiveness. A fully effective programme, requiring no improvement, could score the lowest risk value of Zero.

The total score obtained when assessed across all criteria gives the user an indication of the overall effectiveness of the programme and indicates both the level of improvement required and indicates the areas where such improvements can be made. The total rank field was also colour coded using the traffic light system as an additional visual guide to the control system.

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Table 4: Criteria inclusion justification breakdown

#	Criteria	Justification for Inclusion
1.1	**Is risk assessment conducted for developing the schedule?**	The use of a risk-based approach to scheduling is highlighted in a number of standards and guidance's reviewed: ISO 19011:2018 6.3.2.1 which describes using a risk-based approach to planning an audit The GVP Guideline 'Risk assessment should be documented for planning of audit activity' ISO13485: 2016 Section 8.2.4 states that an audit programme plan should take into consideration the process, the area and previous audit results. ICH Q9 also suggests that quality risk management can be used to define frequency and scope of audits
1.2	**Does it include factors such as scope, time, team.**	ISO 19011:2018 5.2 specifies that each audit must be based on defined objectives, scope and criteria. The requirement for audit criteria, scope and frequency being defined and recorded is also highlighted in ISO 13485:2016 8.2.4 and ISO 9001:2015 9.2
2.1	**Calculate % of CAPA's closed on time**	ISO 9001:2015 and ISO13485:2016 specify the requirement for management to ensure all corrective and correction actions are taken without any undue delay. This is also included based on the output of the industry survey. This criterion also aids in monitoring management commitment, as indicated by O'Mahony. It can also identify opportunity for improvement addressing audit findings.
3.1	**Is tracking performed?**	ISO 19011:2018 states that implementation of the audit programme should be monitored and measured.
4.1	**Are training requirements described in procedure?**	Although all guidance reviewed discuss the competency of auditor, ISO 19011:20185 provides the additional requirement of having sector specific knowledge, completion of an auditor training programme and having technical experience of the management system. It also advises experience acquired under supervision of an experienced auditor. The GVCP Guideline advises that auditors should have both education in the area and relevant work experience
4.2	**Is there evidence of training in area under audit? (technical knowledge)**	ISO 19011:2018 specifies the requirement for relevant technical knowledge of the area under audit and, if not available, that extremal resources with the relevant knowledge maybe used as part of an audit team.
5.1	**Is there a management sign off on reports?**	ISO13485:2016 8.2.4 states that management responsible for the area to be audited should ensure the actions are taken. Area management signatures on an audit report provides evidence for this requirement.
5.2	**Is the data presented at management review?**	This potential failure mode was highlighted based on the number of deficiencies found by HPRA (O'Mahony). Management commitment is also required by 21 CFR 820 and the ISO standards, The requirement for management review is also outlined in ICH Q10 section 3.2.4
6.1	**Description of how audit is performed (as opposed to how it is documented)**	Both EU GMP Chapter 9 and 21 CFR 820 require a procedure to be in place. The ISO standards define the process steps that should be included in the procedure.
6.2	**Clear definitions**	Clear definitions within a procedure provide a guidance to how the self-inspection programme operates Different approaches may be required for different audit types.
6.3	**Clear instruction on steps to be taken when schedule not adhered to.**	ISO 19011:2018 describes the need to evaluate the schedule adherence Any deviation from the schedule may require a review to update to the initial risk assessment performed and therefore should be documented If a risk-based approach is applied when developing the schedule, this must be considered when the schedule is not adhered to.
6.4	**Clear timelines for raising issues, report closure etc**	Documented timelines for the self-inspection programme steps will facilitate in ensuring that it is running smoothly and aid in schedule adherence.

7.1	**Are there tools used supplement to self-inspection programme, e.g. Gemba walks, mini area audits**	Continuous monitoring tools such as the use of checklists, can facilitate the implementation of improvements between the formal process audits. These implementations can aid in reducing the number of findings in formal audits both as part of the programme and external. This can demonstrate improvement within the QMS, inform the risk assessment used to develop the schedule, or justify reduced audit frequency within a self-inspection programme (depending on local regulation requirements).
8.1	**What is the % of findings raised as per schedule e.g. raising CAPA**	There should be a timeframe for when findings are actioned. The adherence to the scheduled timeline determines the output of the programme and informs the risk based approach.
8.2	**Are findings graded based on severity i.e. Minor, Major**	The requirement for grading of findings is detailed ISO 9011 and in ICH Q10. Risk ranking is highlighted as a potential method of audit prioritization. The grading of findings aids in assigning timelines for finding completion and prioritising them. The grading of findings per area can be evaluated from previous years and incorporated as part of a risk assessment when establishing the schedule for subsequent years or evaluation frequency for audit requirement.
8.3	**Clear ownership agreed at audit closure for findings**	The timely closure of CAPA's is assisted if clear and appropriate ownership is assigned. This ties in with criteria 5.1 - management approval of the final report.
9.1	**Is there a review of self-inspection process?** .	EU GMP Chapter 9 requires that self-inspection itself should be examined as part of the programme. Audit of the self-inspection programme can help identify areas of improvement of the process and procedures
10.1	**How many findings have been classified as major within the last year**	This criterion helps evaluate the efficiency of the programme in terms of identifying process improvements.
10.2	**No. of findings from regulatory inspection which have been previously recorded in an internal audit**	This criterion helps evaluate if the current programme is efficient. A low score on this criterion indicates that the findings raised as part of a self-inspection programme have been managed well and a potentially verifies the root cause of the given finding.
10.3	**Is there an "Lessons learned" meetings following the completion of a self-inspection schedule?**	As per recommendation in ISO 19011 Section 5.7 *'reviewing and improving audit programme'* the lessons learned from programme review should feed in as inputs towards programme improvement. This section of the ISO standard also specifies areas that should be reviewed. In addition, ICH Q9 guide for risk management highlights audits as a planned event which should be risk reviewed in order to take into account new knowledge and experience (ICH Q9)

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The SI-PEA Tool

Control System:	If Total Rank Score >60, major improvements to internal audit program are required ● If Total Rank Score >30, deficiencies in the internal audit program ● If Total Rank Score <30, areas of improvement identified for audit program effectiveness ●			
Internal Audit Program Effectiveness Assessment				
Item	**CRITERIA**	**Potential Failure Mode**	**Rank Rating**	**Rank**
1	Scheduling	Is risk assessment conducted for developing the schedule.	If yes rank = 0 If no rank = 5	
		Does it include factors such as scope, time, team.	If yes rank = 0 If no rank = 5	
2	Timely closure of CAPAs	Calculate % of CAPA's closed on time	If all closed rank = 0 If 80-100% rank = 1 If 60-80% rank = 2 If 40-60% rank = 3 If 20-40% rank = 4 If 0-20% rank = 5	
3	Tracking	Is tracking performed	If yes rank = 0 If no rank = 5	
4	Auditor suitability	Is training requirements described in procedure	If yes rank = 0 If no rank = 5	
		Is there evidence of training in area auditing (technical knowledge)	If yes rank = 0 If no rank = 5	
5	Management commitment	Is there management sign off on reports	If yes rank = 0 If no rank = 5	
		Is the data presented at management review	If yes rank = 0 If no rank = 5	
6	Procedure	Description of how audit is performed (as opposed to how it is documented)	If yes rank = 0 If no rank = 5	
		Clear definitions e.g. corporate audit counts as internal audit or not	If yes rank = 0 If no rank = 5	
		Clear instruction on steps to be taken when schedule not adhered to	If yes rank = 0 If no rank = 5	
		Clear timelines for raising issues, report closure etc.	If yes rank = 0 If no rank = 5	
7	Use of independent audit tools	Are there tools used supplement to self-inspection program, e.g. Gemba walks, mini area audits	If yes rank = 0 If no rank = 5	
8	Findings	% of findings raised as per schedule e.g. raising CAPA	If all raised on time rank = 0 If 80-100% rank = 1 If 60-80% rank = 2 If 40-60% rank = 3 If 20-40% rank = 4 If 0-20% rank = 5	
		Are findings graded based on severity i.e. Minor, Major	If yes rank = 0 If no rank = 5	
		Clear ownership agreed at audit closure for findings	If yes rank = 0 If no rank = 5	
9	Audit of Self inspection program	Is there a review of self-inspection process	If yes rank = 0 If no rank = 5	
10	Efficiency measurement	How many findings have been classified as major within the last year	If >5 rank = 5 If >1 rank = 3 If none rank = 0	
		No. of findings from regulatory inspection which have been previously recorded in an internal audit	If >5 rank = 5 If >1 rank = 3 If none rank = 0	
		Is there an actions learned meetings following the completion of a self-inspection schedule	If yes rank = 0 If no rank = 5	
			Total Rank	0

Pilot Study – Self-Inspection Programme Effectiveness Assessment (SI-PEA) Tool

The assessment tool was piloted in two companies to assess its practicality and whether it generated information that could be helpful to the organisation in determining the effectiveness of the programme. The study was conducted in companies who use self-inspection to assess the effectivity of the QMS. In each case the tool was assessed by the persons responsible for the programme.

Company A acts as a supplier of laboratory equipment and reagents and as a provider of calibration and contract testing services to the pharmaceutical industry. The QMS at Company A is a hybrid of paper and electronic based documentation and is designed to meet the requirements of ISO 9001:2016 and ISO 17025:2017 *General Requirements for the Competence of Testing and Calibration Laboratories* [20]. Company A is audited by the Irish National Accreditation Board (INAB) and the British Standards Institution (BSI). This company was considered as a pilot site because it also tested the usefulness of the tool as a monitoring tool for assessing the QMS of critical suppliers.

Company B is a contract manufacturer for both the pharmaceutical and medical device sectors and therefore complies with the regulations of both sectors. Company B is audited by the US FDA, HPRA, and SGS. Due to its activity as a contract manufacturer, is also has numerous critical-to-business customer audits. This company considers findings by customers or regulatory inspectors as a significant risk and was, therefore, also a useful pilot site.

Prior to completing the study, the participants in both companies were given background details to each criterion as per Table 4. Each participant completed the tool during a virtual meeting. This allowed the researcher to monitor the process in addition to answering any queries. The results obtained from each participant were not shared with the other participant.

The functionality of the tool was assessed based on the following criteria.

1. Successful completion of all required fields and ease of use
2. Production of a realistic and reflective effectiveness score for each company

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3. Usefulness in identifying areas of improvement / gaps in current programme is clearly identifiable to each user.

Outcome of Pilot Study

The tool demonstrated full functionality with respect to the established criteria. With access to the relevant information, the users took between 15-20 mins to complete the tool, confirming ease of use. While there were some questions and clarifications, the users expressed no difficulties. The users were able to select data from a drop-down menu under the 'rank' column. Once all ranks were selected, the total rank score was calculated automatically.

The total risk rank for Company A was 25, falling in the category of <30. This determined that overall, the programme was satisfactory, with some opportunities for improvement. The total rank for Company B was 28 which is also in the green risk category as per control system rank score indicator. This was consistent with the maturity of the QMS in both operations.

However, both scores indicated opportunities for improvement. The areas of improvement identified were as follows;

1. Scheduling - Neither company took a risk-based approach to determining the audit schedule – a key reason for regulatory findings

2. Timely closure of CAPA's – Both companies identified that CAPAs closure this was an area of further improvement as indicated by the SI-PEA tool

3. Procedure – Both companies identified areas of improvement within their procedures. Company A did not have clear descriptions of how audit is performed. Neither company documented instructions on required steps if schedule is not adhered to.

4. Findings – Company B identified a gap with respect to clear ownership agreement of audit findings. This potentially contributes to timely CAPA closure being below target.

5. Efficiency measurement – Both companies identified that there are no 'lessons learned' reviews following the completion of a self-inspection schedule.

Each participant found the tool useful in identifying areas of improvement, it was considered easy to use with clear instructions. When requested to suggest improvements of the tool, both recommended incorporating a prompt, prior to giving final rank score, if a section is not completed. This assures that this omission is not overlooked.

Conclusion

Regulatory guidance and international standards require that Self Inspections be performed to monitor the implementation of the QMS and to identify opportunities for improvement. The most common method of establishing whether the programme is effective has been to monitor adherence to schedule and the output in terms of findings and the implementation of effective CAPA actions. While these criteria are appropriate, they do not monitor the full expectations of the programme.

This research has examined these expectations comprehensively and has developed a Self-Inspection Programme Effectiveness Assessment (SI-PEA) tool to monitor all the expected criteria of the programme's objectives. The tool incorporates a risk score which can be used to track improvement of the programme over time. It can also identify potential areas of improvement within a self-inspection programme and demonstrate both effectivity and improvement. It is easy to populate, use and interpret. The tool created should first establish compliance to all regulatory expectations since without compliance a self-inspection program cannot be effective. The SI-PEA too can be further customised depending on a companies activities however this should not result in removal of the existing factors discussed in the tool.

When used to report the effectiveness of the programme to Management Review, it could assist in establishing the effectiveness of the pharmaceutical quality system, a key requirement to availing of any regulatory reliefs as described in Annex 1 of ICH Q10.

The tool has further potential to monitor both maturity and effectiveness. The SI-PEA tool is a preliminary model some further work to develop further criteria would develop the latter. In addition, further development could also assist with monitoring the Self-Inspection

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effectiveness of a suppliers QMS or of a provider of outsourced activity. It also has the potential to be used by regulatory inspectors.

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