BioPhorum

SINGLE-USE SYSTEMS CHANGE-NOTIFICATION SCORECARD SURVEY

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Bio-Process Systems Alliance

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BioPhorum
Sam Denby

About BioPhorum

The BioPhorum Operations Group's (BioPhorum's) mission is to create environments where the global biopharmaceutical industry can collaborate and accelerate its rate of progress, for the benefit of all. Since its inception in 2004, BioPhorum has become the open and trusted environment where senior leaders of the biopharmaceutical industry come together to openly share and discuss the emerging trends and challenges facing their industry.

Growing from an end-user group in 2008, BioPhorum now comprises 53 manufacturers and suppliers deploying their top 2,800 leaders and subject matter experts to work in seven focused Phorums, articulating the industry's technology roadmap, defining the supply partner practices of the future, and developing and adopting best practices in drug substance, fill finish, process development and manufacturing IT. In each of these Phorums, BioPhorum facilitators bring leaders together to create future visions, mobilize teams of experts on the opportunities, create partnerships that enable change and provide the quickest route to implementation, so that the industry shares, learns and builds the best solutions together.

1.0

Executive summary

This survey is a key tool for continuous improvement in the ongoing mission of the BioPhorum disposables program to achieve at least 90% right-first-time supplier change notifications for single-use systems (SUS) used in the bioprocessing industry.

It is anticipated that achieving this goal will provide significant cost and time savings, improve quality and provide confidence to more rapidly adopt single-use systems, and the flexibility they provide as a strategic tool for biopharmaceutical manufacturers.

This is the first time this survey has been run and it therefore establishes a baseline for the performance of change notifications for single-use systems within the bioprocess industry.

Results of the survey highlight that at present the industry is operating at 50 to 75% right-first-time supplier change notifications in four key aspects measured in the survey (categorization and timing, change description effectiveness, data package quality and workflow/ communication effectiveness). The target among biomanufacturers and supply partners is to increase this to greater than 90%.

The survey results reveal that there appears to be limited alignment of what constitutes 'good' in respect of data packages, which presents a key challenge. The BioPhorum supplier change notification workstream is seeking to address this by producing content to standardize data package recommendations. Ultimately, the team believes that addressing this will drive significant improvement in workflow effectiveness for change notification.

Moving forward, the intention is to use this tool to demonstrate the benefits that alignment of change-notification practices brings and the industry's progress in this continuous improvement initiative. The next step will be to run this survey with a broader audience, and you are encouraged to invite your customers, your suppliers and their suppliers to participate in this survey.

2.0

Introduction

Since 2015, the BioPhorum/BPSA Single-Use Systems Change Notification team have been working to develop a standardized, industry-wide framework for the notification of changes to single-use systems used in the bioprocessing industry. In 2015 the team identified the challenges posed by current ways of working and the need for an industry-wide solution (White and Ott, 2015). The team developed a proposed methodology and published an industry proposal for change-notification practices for single-use biomanufacturing systems (Carter et al., 2017a; Carter et al., 2017b). A significant number of member companies expressed interest in implementing these practices and deriving benefit from them.

Following publication of the paper in 2017, it was clear that there were challenges in the change-notification processes for single-use biomanufacturing systems. The industry proposal for best practice was written to improve change-notification processes across the industry. The team evaluated the situation and acknowledged that while there was a collective understanding that the process could be improved – and areas for improvement had been identified – there was no mechanism by which to survey and measure the state of change notifications for single-use biomanufacturing systems. Furthermore, the team identified the need to monitor whether the ways of working outlined in the 2017 best practice proposal were effective in improving the status of change notifications for these products. To this end, the team agreed to periodically run a scorecard survey to establish how effective the proposed best practices are in bringing about improvements to change-notification processes in the industry.

2.1 Purpose

The purpose of the survey is to understand the aggregated perception of the industry from drug sponsors through the supply chain. Currently, the survey is designed to capture input from component manufacturers and single-use system integrators, although it could be extended through the supply chain.

Each time the survey is run, participating companies are requested to complete the survey by providing one collated response from their company. The purpose of the survey hosted by BioPhorum is not for companies to complete the scorecard survey separately for each supplier and customer interaction. Companies are welcome to use the scorecard to monitor or improve specific relationships as part of their quarterly business review or other process but should not report the measurement of a single relationship to BioPhorum.

A central tenet of the survey design is that it should be easy to complete and should not provide an unnecessary administrative burden. During the design of the scorecard survey, it became apparent that very few companies have readily available hard metrics around how much rework is necessary during a change notification, how effectively changes are categorized or the completeness of data packages provided. Furthermore, while most companies were able to identify how many changes they had handled in total during a given time period and what percentage of those were attributable to single-use systems, most companies were not able to provide hard data about how long it had taken them to handle changes, how many associates had been involved or whether this varied by 'severity of change'. This may be something to review as best practices become embedded through the industry and there is increasing standardization on how changes should be categorized.

For the moment, what is most important is understanding the direction of trends relating to change notification for single-use systems and whether the proposed practices are having the desired effect. To that extent, the team agreed that asking each company for consolidated feedback from the associates handling the change-notification process should provide a good measure of the current status of single-use change notifications within the industry.

This is the first time the survey has been run and so the purpose is to establish a baseline of the current status of change notification among the companies participating with the workstream.

3.0

Questions asked

3.1 Respondent profiling

Some standard questions were asked to enable follow up and clarification (name of respondent, respondent's organization). This information will not be published and all data shown is aggregated and anonymized.

For this round of the survey, respondents were profiled by role (quality assurance (QA), supplier quality, regulatory affairs, process development, technical services/ manufacturing sciences and technology (MSAT), procurement, or other (specify)). Where a cross-functional team responded, it was possible to select multiple roles. Respondents were further profiled by how their organization's business self identified (drug sponsor, contract manufacturing organisation (CMO), supplier of SUS assemblies, supplier of SUS components, supplier of SUS raw materials).

3.2 Quantity of SUS change notifications

Respondents were asked how many change notifications they had received (drug sponsors) and issued (supply partners) for single-use systems in the previous year. They were also asked to indicate whether the trend in these numbers was increasing or decreasing.

3.3 Quality of SUS change notifications

Questions were asked to identify respondents current and desired experience of change notification. In each section, questions were asked in pairs – how would you rate your current experience and what rating do you need to achieve?

In all cases, companies were asked to provide a score between 0 and 10 for their experience in relation to each question with 0 being extremely negative and 10 being extremely positive. A framework is provided in Performing this survey has been a very useful exercise, providing some great insights into current areas of convergence and divergence of companies' experiences with change-notification process throughout the biopharmaceutical supply chain. Importantly, since this is the first time the survey has been run it has established a baseline in terms of current performance of the change-notification processes employed by respondent companies. It has highlighted significant differences in the number of change notifications drug sponsors are handling for single-use systems. Establishing the current status of these practices is important as the intention of the team is not to increase the number of change notifications received, but rather to identify and focus on the change notifications likely to have the most impact.

The survey has also been very useful in uncovering a 'revealed problem'. End-users consider data packages to be highly impactful to the change-notification process. A good data package, delivered with the change notification, provides the leanest workflow and minimizes the need to follow up with additional questions to the supplier. Since the drug sponsors are the ultimate customers in this supply chain, they will typically drive rework and requests for additional information from the supply chain. Figure 8 shows that there is a lack of agreement between drug sponsor companies on the quality of the data packages they currently receive. Reflecting on this, the team acknowledged that at the time of the survey, little work had been carried out to define what constitutes 'good' with respect to single-use system change-notification data packages. Without alignment between drug sponsors it is very difficult for supply partners to meet expectations as these may differ between drug sponsor companies. The impact of this on timelines may be exacerbated when requests for additional data need to be passed on from tier 1 suppliers through the supply chain. Team agreed to a subgroup composed of both drug sponsors and suppliers working to develop guidance on data package recommendations.

Moving forward, the survey has allowed companies participating in the BioPhorum initiative to measure the current status of key aspects of the change-notification process that their best practice is intended to address. This forms a baseline against which continuous improvement efforts can be measured. A key revealed problem has been identified prompting the group to develop content to address this. The intention is now to run this survey with a broader audience and continue to measure the impact that our best-practice proposal is having on change-notification single-use systems within the bioprocessing industry. As more companies implement this practice, when this survey is repeated it will be possible to measure whether the goals of the collaboration (>90% right-first-time change notifications) are being met or whether there is a need to correct the course by adapting ways of working or revising published tools and guidance.

3.3.1 Categorization and timing

The questions in this section are designed to understand whether the complexity/impact of the change has been well understood and effectively incorporated into the change notification. In the case of drug sponsors this will be directly based on the changes they have received. For supply partners the aim is to understand how effectively they believe they are categorizing changes, typically based on feedback (or lack of feedback) from their customer base.

The two questions asked in this section are:

How would you rate your experience of Categorization and Timing? (0–5)

What rating do you need to achieve for Categorization and Timing ? (0–5)

3.3.2 Change description effectiveness

The questions in this section are targeted at understanding whether the change has been described effectively enough to allow an end-user to make a right-first-time impact assessment for the change, without needing to revert to the supplier for additional information.

The two questions asked in this section are:

How would you rate your experience of change description effectiveness (and anticipated end-user-impact assessment)? (0–5)

What rating do you need to achieve for change description effectiveness (and anticipated end-user-impact assessment)? (0–5)

3.3.3 Data package quality

This section addresses the availability and quality of data packages supporting a change notification. Questions in this section are designed to understand whether data packages are provided without request and whether it is possible to use the available data packages without requesting additional information.

The two questions asked in this section are:

How would you rate your experience in relation to data package quality? (0–5)

What rating do you need to achieve in relation to data package quality? (0–5)

3.3.4 Workflow/Communication effectiveness

This section addresses the effectiveness of both the overall workflow and communication about the change. Change notifications and pre-notifications should be provided in line with the guidance set out in the industry proposal for change-notification practices associated with single-use biomanufacturing systems (Carter et al., 2017b; Carter et al., 2017a). Where the workflow is effective, any rework should be minimal, allowing notification and implementation of changes in a timely manner and in line with the guidance for each level of change.

The two questions asked in this section are:

How would you rate workflow/communication effectiveness? (0–5)

What rating do you need to achieve in relation to workflow/communication effectiveness? (0–5)

3.3.5 Overall satisfaction

This question aims to understand how organizations' perception of the change-notification process for single-use systems is evolving over time. Respondents were not asked what their desired satisfaction level would be.

How would you rate your overall satisfaction with the single-use change-notification process? (0–5)

3.3.6 Ranking

Questions in this section are designed to identify the most valuable aspects of change notification to drug sponsors. Impactful areas that are relatively easy to achieve represent quick wins.

Respondents were asked to rank the four aspects (categorization and timing, change description effectiveness, data package quality, workflow effectiveness) from 1–4, as follows:

Please rank categorization and timing, change description effectiveness, data package quality and workflow effectiveness from most (4) to least (1) challenging.

Please rank categorization and timing, change description effectiveness, data package quality and workflow effectiveness from most (4) to least (1) impactful.

4.0

Development of the survey

The survey was developed by the change-notification workstream. The intention is to use this survey over the coming years to assess how effectively the best practice principles are being embedded and sustained throughout the industry and how positive the impact on change notifications for single-use biomanufacturing systems has been.

4.1 Guidance on completing the survey

Ideally the team wanted to use key performance indicators (KPIs) based on hard data collected by participating companies. Due to the complex nature of this co-implementation, it was not possible to agree hard, data-based key performance indicators that were readily available. All companies within the workstream have rigorous and effective change management processes and have a sense that they are frequently needing to request additional data, that rework is often required, or that there is opportunity to improve the process. Many companies handle changes through cross-functional teams and do not typically record how many full time equivalent (FTE) hours are associated with handling a given change, how complete the data package was, how long the change should have taken to implement and the time it actually took to implement. If companies have any of this data, there is no agreement on how it should be measured so trying to compare hard data from different companies would be challenging. As companies adopt these practices, development of hard, data-driven KPIs may be a consideration for the future.

While hard KPIs may not be available, practitioners of change notifications and leaders of these functions within companies do have a sense of how their suppliers and customers are performing in respect to each of the aspects covered in this survey. By asking each organization to provide an aggregated score, the organization has the opportunity to survey a representative group of associates from different functions. By surveying a cross functional team differing views and experiences related to particular change notifications are balanced out. To support reaching a unified score for the company and to provide some level of moderation between company responses (preventing overly optimistic or pessimistic views from biasing outputs), the scorecard framework was developed (see Performing this survey has been a very useful exercise, providing some great insights into current areas of convergence and divergence of companies' experiences withchange-notification process throughout the biopharmaceutical supply chain. Importantly, since this is the first time the survey has been run it has established a baseline in terms of current performance of the change-notification processes employed by respondent companies. It has highlighted significant differences in the number of change notifications drug sponsors are handling for single-use systems. Establishing the current status of these practices is important as the intention of the team is not to increase the number of change notifications received, but rather to identify and focus on the change notifications likely to have the most impact.

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Appendix 1

It is important to highlight that this scorecard framework is intended to guide thinking and support a discussion to reach a consensus around what score an organization provides in response to the questions. It is not intended that companies collect data to justify that they are meeting specific percentages laid out. There is also some room for interpretation. For example, where a supplier issues 10 notifications in a year to 50 customers and receives one report for nine of those changes that the categorization of those changes was not correct and 30 reports for one of those changes that the categorization was not correct this could reasonably be interpreted as a score of 7–8, with the supplier considering that they are categorizing changes correctly 75–90 % of the time.

5.0

Results

5.1 Respondent profiles

There are a number of ways in which respondents can be grouped. For this first survey it was considered that no companies have yet implemented the practices.

5.1.1 Respondent company type

A total of 16 responses were collected, including two responses from one drug sponsor and two responses from one SUS assembly manufacturer. One SUS assembler response was considered an outlier and will be discounted from analysis and discussed separately (see section 5.3.1).

Figure 1: 16 Companies responded to the survey, eight of these self-identified as drug sponsors, six as suppliers of SUS assemblies and two as suppliers of SUS components

No responses were collected from companies identifying primarily as CMOs or suppliers of SUS raw materials. There were only two responses from companies identifying as suppliers of SUS components and consequently caution must be taken in drawing conclusions. The chart in Figure 1 (or a similar chart) will be used as part of a dashboard to monitor uptake of the proposed change-notification practices.

5.1.2 Respondent roles

In general, respondents tended to be from quality roles (QA, supplier quality). Responses from technical services and cross-functional teams were higher among drug sponsors than other groups.

Figure 2: Cross-functional teams were used by three drug sponsors. 'Other' functions identified by suppliers included regulatory support and marketing/product management roles.

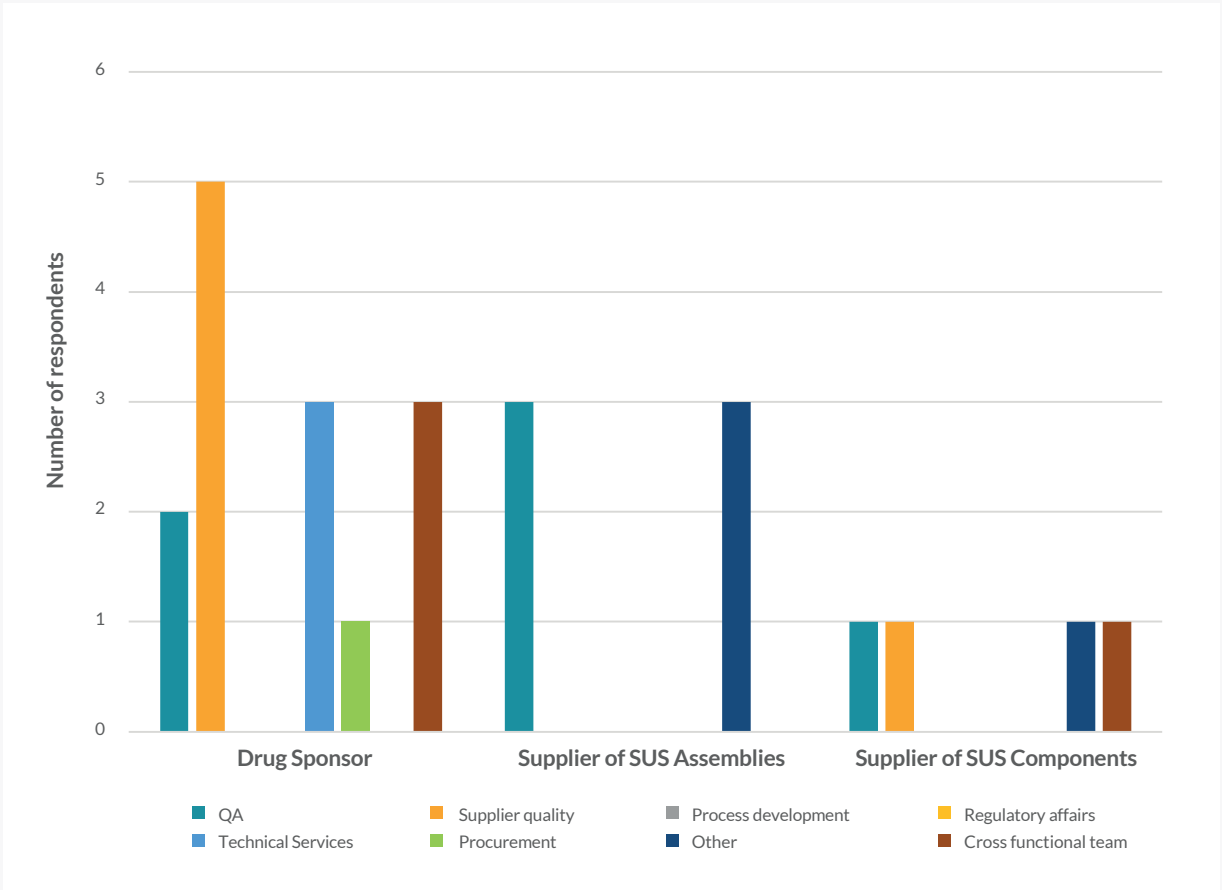


Figure 2 shows that procurement and regulatory functions are underrepresented from all respondent companies. Process development functions were not surveyed at all, which may reflect the rise of MSAT functions as technical custodians of chemistry and manufacturing control (CMC) activities.

Several respondents in each respondent group identified as 'Other':

Drug sponsor – one respondent identified as 'global technical operations' and was included under technical services.

Supplier of SUS assemblies – one respondent identified as 'regulatory support', two respondents identified as 'marketing operations'.

Supplier of SUS components – one respondent identified as 'product management'.

This probably represents a cross-section of individuals within a company who are engaged with change notification for single-use systems and demonstrates that a number of stakeholders with diverse views are likely to be engaged with notifying and reviewing changes.

5.2 Quantity of SUS changes handled

5.2.1 Mean number of SUS changes handled

Respondents were asked to indicate how many change notifications relating to single-use systems they handle on an annual basis. The simplest snapshot of this is the mean number of SUS changes handled (reviewed or notified) by each respondent group.

Figure 3: Mean number of SUS changes handled by different respondent groups. A clear trend is seen, with an increase in the number of change notifications issued/received as products move from component manufacture, through assembly to use.

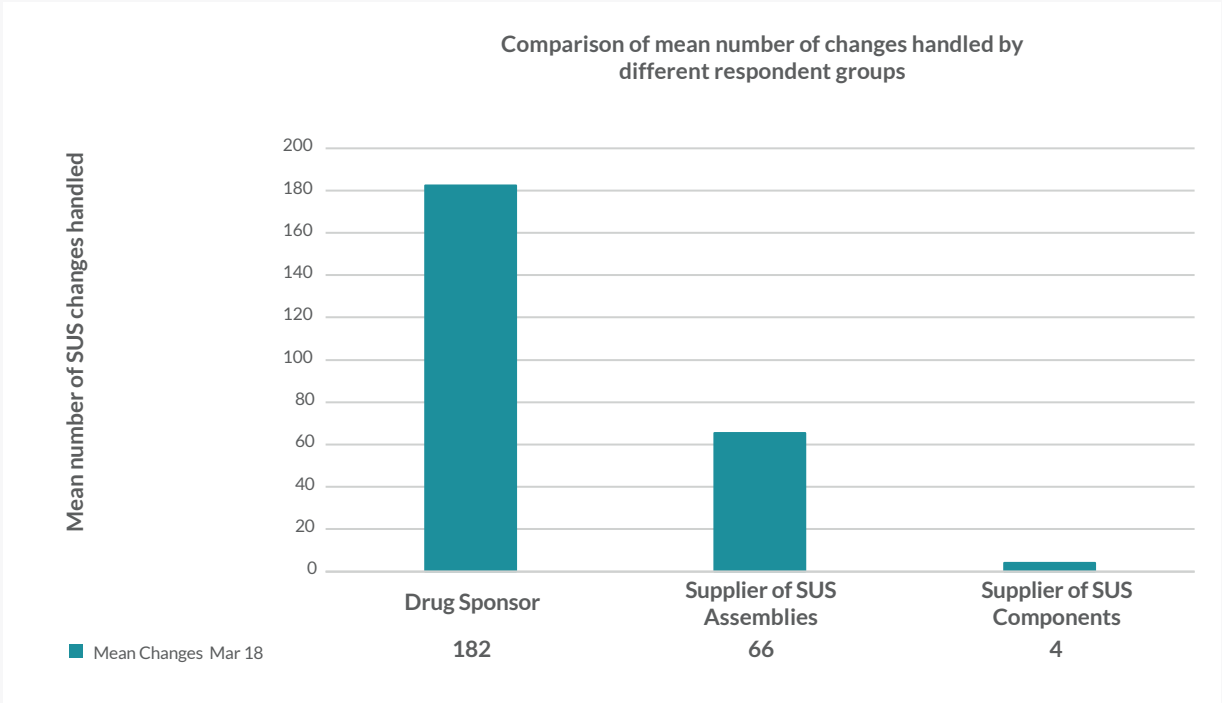


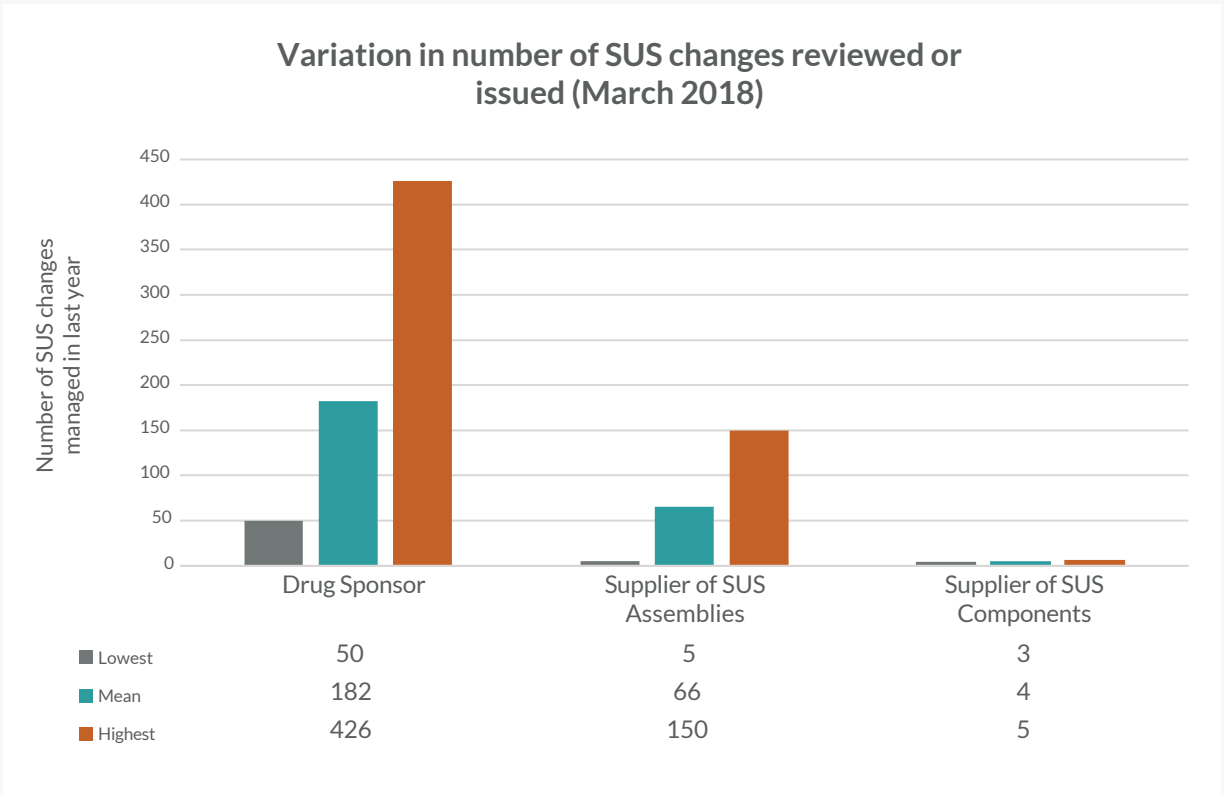
Figure 3 shows how the number of change notifications for single-use systems appears to increase or propagate through the supply chain with significantly greater numbers of changes being handled by drug sponsors than any other group surveyed. To an extent this may be expected, since there is an approximately three-fold difference between the number of changes handled by drug sponsors versus suppliers of SUS assemblies. If a drug sponsor is using multiple sourcing (two or three vendors) then this ratio would make sense. The high level view shown in Figure 3 will be reported as part of the dashboard on the BioPhorum website.

Further breakdown of these numbers is provided in section 5.2.2 and will be monitored in the full report provided for each iteration of the survey.

5.2.2 Variability in number of SUS changes handled

One striking aspect of the survey was the difference in the number of changes reviewed or issued by companies. There are several factors that should be taken into consideration. For drug sponsors, respondents from global functions are likely to see more changes than those with more local responsibility. Larger companies with a broader product portfolio are likely to have more changes to review. Similarly, for suppliers, those with larger or more complex portfolios are likely to issue more changes than those with smaller or less complex portfolios.

Figure 4: Variability in the number of changes related to single-use systems reviewed by drug sponsors or issued by suppliers over the last year.



Despite these factors, it appears that there is an eight-fold difference between the lowest and the highest number of changes reviewed by drug sponsors and a 30-fold difference in the number of changes (lowest to highest) initiated by suppliers of single-use assemblies. This is likely, at least in part, to be caused by differences in what is and is not notified/reviewed between companies. Publication of a standardized decision tree to support categorization of changes should go some way towards harmonizing the approach taken by different companies.

A very small number of component suppliers responding to this survey and it may be that the average number of changes issue by component suppliers is somewhat higher. Based on the numbers reported in the survey it does seem that a very small number of changes at the component manufacturer level propagates to a very large number at the drug sponsor level. This is something the team may wish to revisit, along with the notion of a common change identifier to allow drug sponsors to know/understand when multiple changes presented from SUS assemblers have the same root at the component or raw material level.

5.3 Quality of SUS change notifications

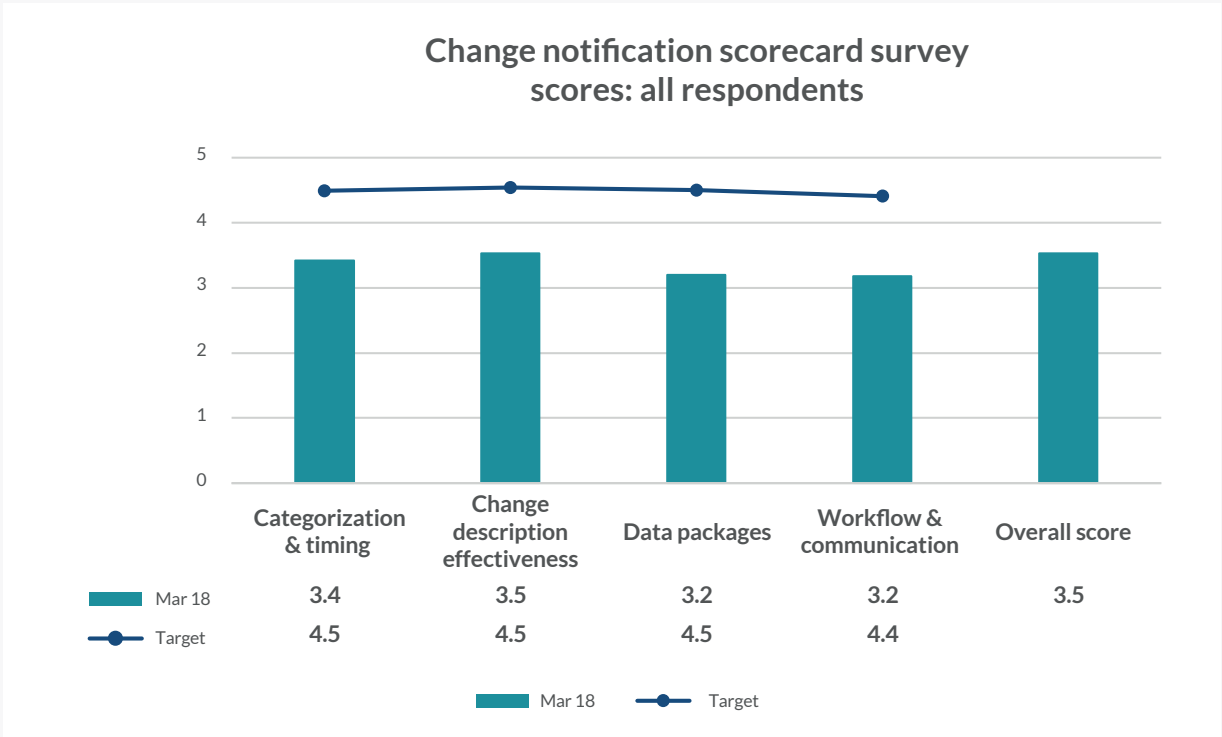
5.3.1 Outlier

One response from suppliers of SUS assemblies appeared to be an outlier with scores significantly lower than those provided by their peers. The objective of the survey was to understand how suppliers scored themselves on the notifications they provide to their customers. Upon discussion, it emerged that the outlier had provided scores based on the notifications they receive from their suppliers and consequently, the outlier's scores were removed from analysis with the SUS assembly suppliers. In some instances, the outlier results are shown separately as the scoring does reveal potential challenges that may need to be addressed for these best practices to become embedded and sustainable throughout the value chain. Notably, working with tier 1 or tier 2 suppliers may not be sufficient to improve the overall performance.

5.3.2 Mean rating for each aspect

Figure 5 shows the mean score across all respondents for each aspect surveyed. Generally, there is a reasonable level of satisfaction with the current status, although with a desire to improve further in all areas.

Figure 5: Mean industry score and target for each aspect of change-notification practices surveyed

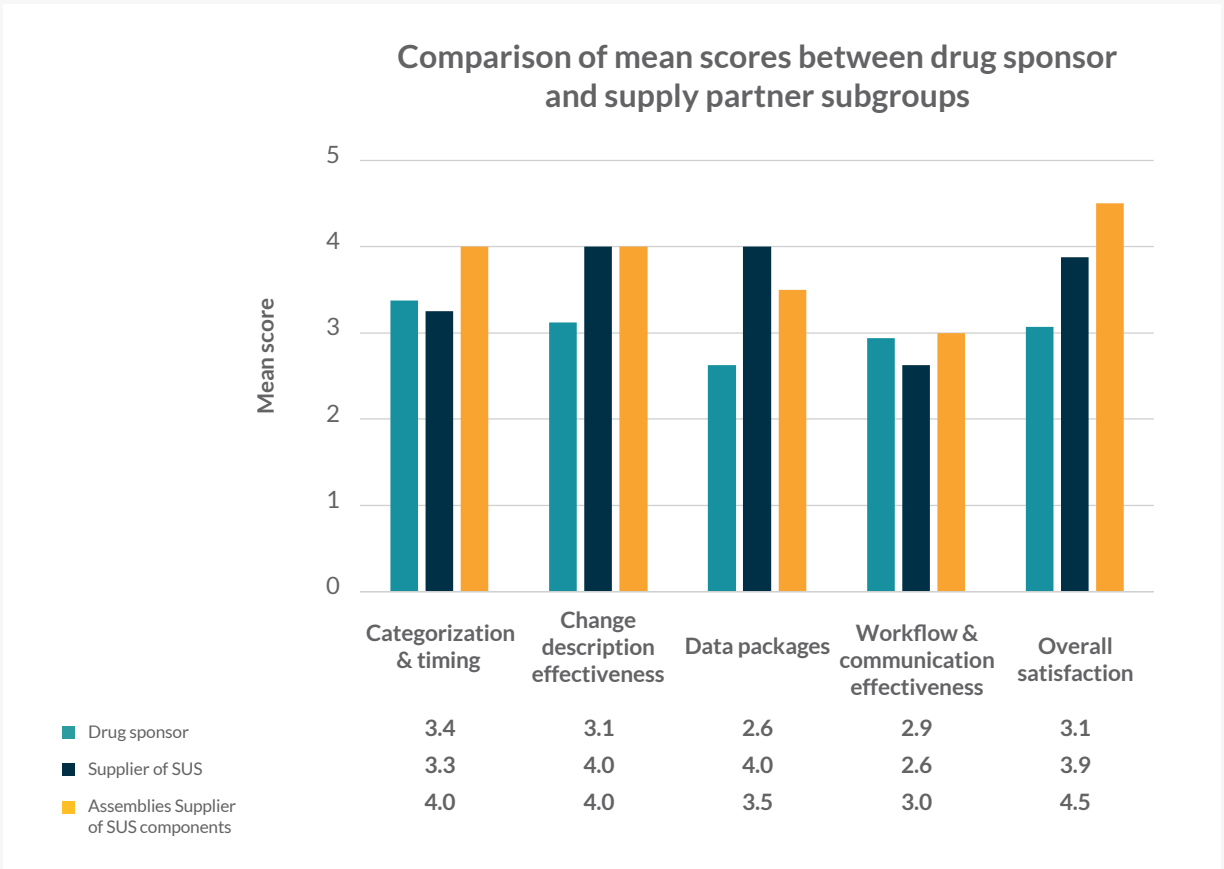


The team has focused most closely on categorization and change description effectiveness and this is perhaps reflected in the results. Analysis of variability between and within subgroups is shown in subsequent sections and reveals areas of focus for the team.

5.3.3 Mean scores for each aspect surveyed in different subgroups of the supply chain

Although the mean scores for each aspect of change notification surveyed are relatively high, there is some difference in scoring between drug sponsors and the supply base. Generally, drug sponsors score the current state less positively than supply partners. In part, this may be related to drug sponsors being asked to score based on what they receive and supply partners being asked to score based on what they provide.

Figure 6: Comparison of mean scores between respondent groups for each aspect surveyed



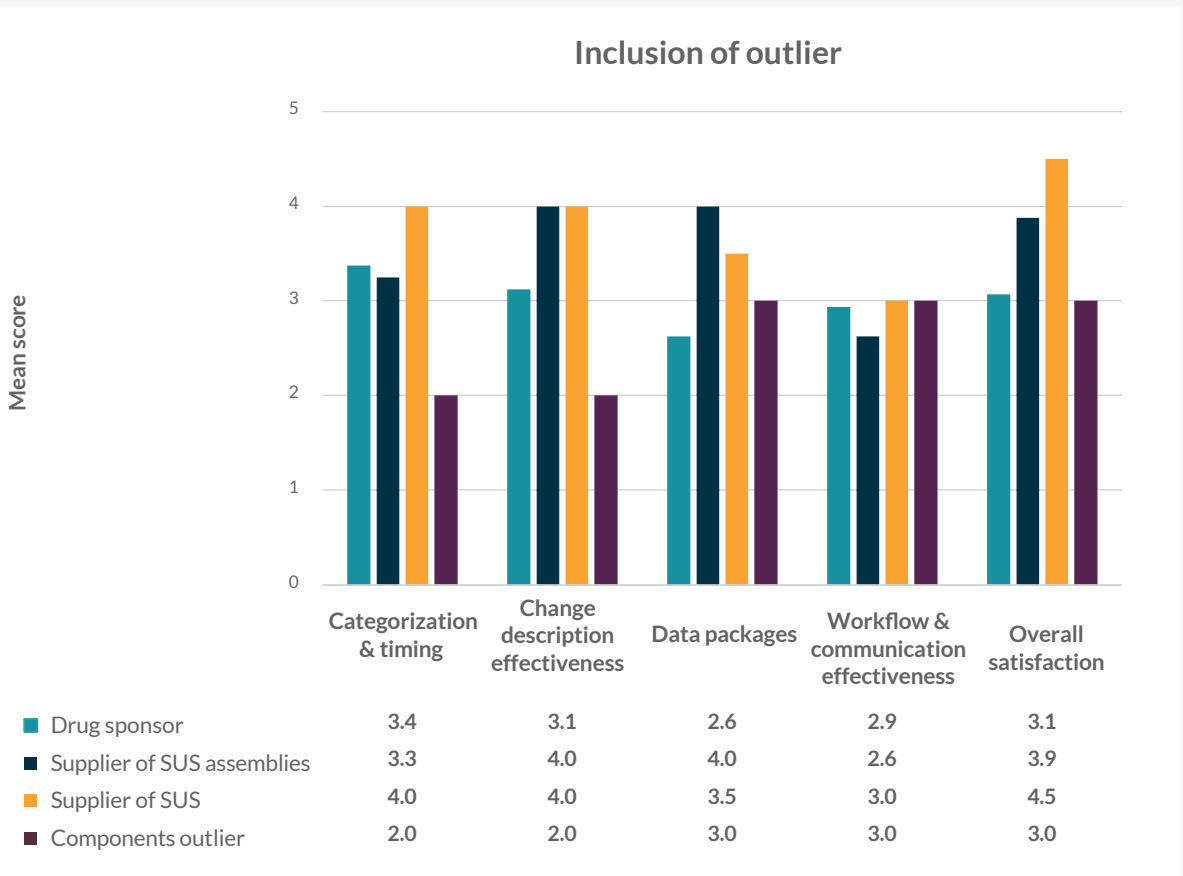
What is particularly notable is a difference in scoring between drug sponsors and supply partners in relation to data package quality. This discrepancy will drive challenges in relation to workflow effectiveness. What is clear is that investigating the discrepancy in expectations for data packages will be important in improving the general performance of change notifications for single-use systems. Perhaps reassuringly, this is an area the team had previously identified but not yet focused on. Conversely, areas such as categorisation and timing, which have received significant attention, score much more highly and much more consistently. While these are still benchmarking data, it is an early indication that improvements have been made in areas on which the team has already focused.

5.3.4 Inclusion of outlier data

Inclusion of the outlier mentioned previously, where one supply partner responded based on the quality of change notifications they have received rather than issued, provides some valuable insights.

When scoring their supply base, this supplier of SUS assemblies indicated very poor performance across all aspects. This is based on only one data point and may not be a true reflection of the situation seen by other SUS assembly suppliers. However, it provides an indication that drug sponsors will not be able to improve the performance of the change-notification system on their own, and it is likely to be necessary to engage as broad a cross-section of the SUS supply chain as possible. It highlights the importance of continuing efforts to engage lower-tier suppliers in this way of working and in adopting the tools and practices developed by the workstream.

Figure 7: Comparison of mean scores between respondent groups including outlier



5.3.5 Variability within respondent groups

As well as differences in responses between groups, significant differences were observed in experience within groups. This was most obvious in the drug sponsor grouping.

Figure 8 shows variability within the drug sponsor group. Although current scoring is likely to vary due to differing experiences and expectations, there is at least a three-point difference between the lowest and highest score for each aspect with a seven-point difference for data package quality and workflow/communication effectiveness. Based on comments received data package quality is, in many cases, linked to workflow and communication effectiveness with several respondents commenting that data packages must be requested multiple times and/or are incomplete.

It is clear that work remains to harmonize further drug sponsors' expectations, particularly in relation to data package quality. Those areas which have had more focus (e.g. categorization and timing) have more alignment in terms of scoring. It will be important for drug sponsor companies to maintain engagement with the process of sustaining and embedding these change notification practices. If expectations are aligned and defined between drug sponsor companies, the likelihood of the supply chain being able to meet the expectations increases.

Figure 8: Low, mean and high scores for responses received from drug sponsors

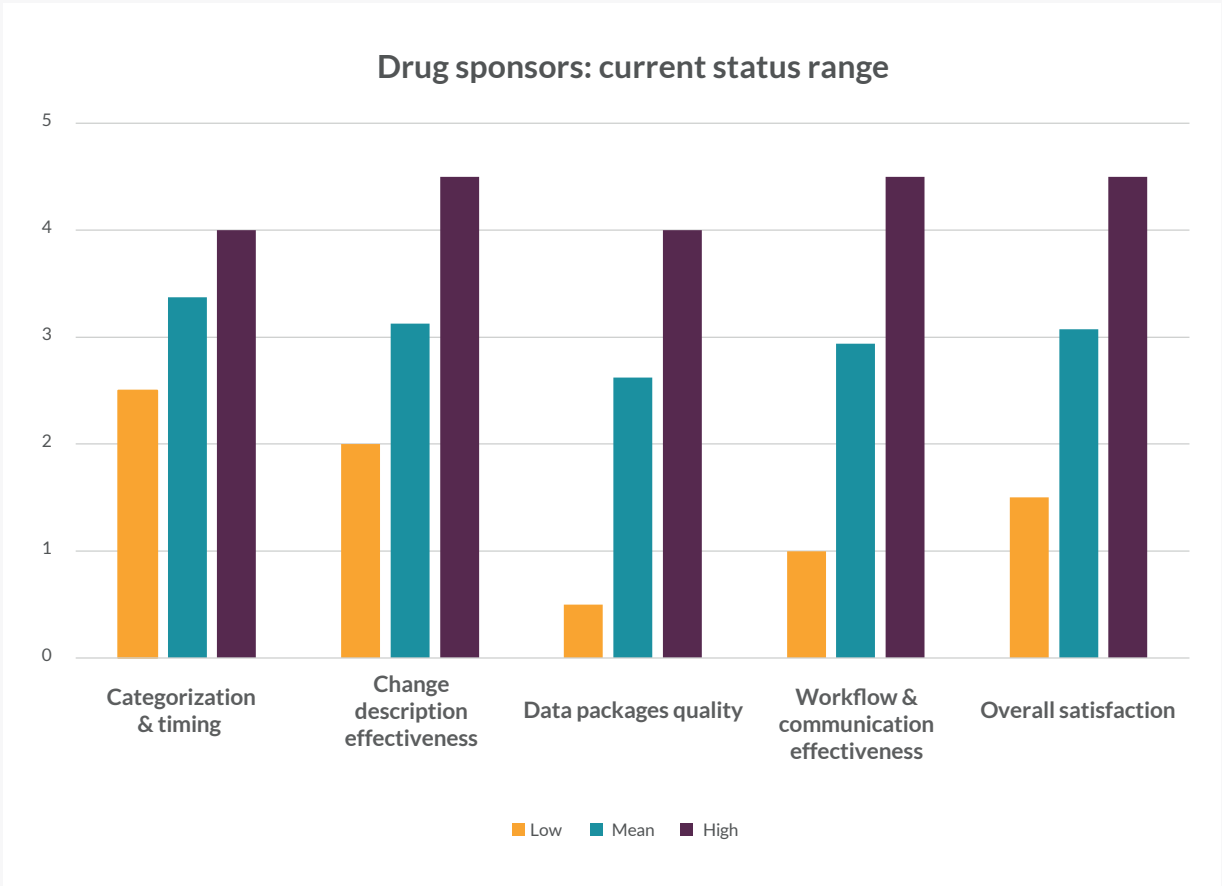


Figure 9: Low, mean and high scores for responses received from suppliers of SUS assemblies

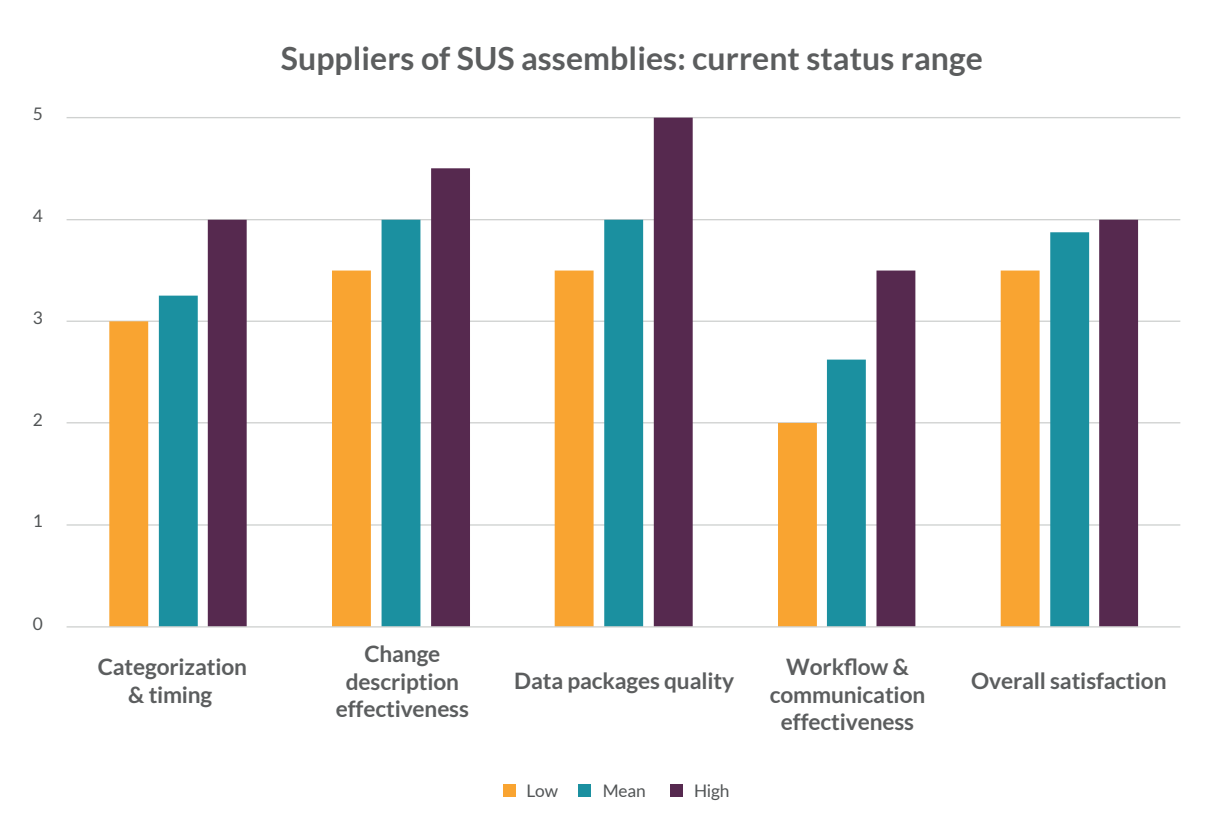


Figure 9 shows aligned scoring between suppliers of SUS assemblies on the quality of the notifications they supply. This establishes a good benchmark, but it will be important to continue monitoring this to ensure there is adequate feedback from drug sponsors to supply partners so they can continue improving and aligning expectations with what is provided.

Figure 10: Low, mean and high scores for responses received from suppliers of SUS components

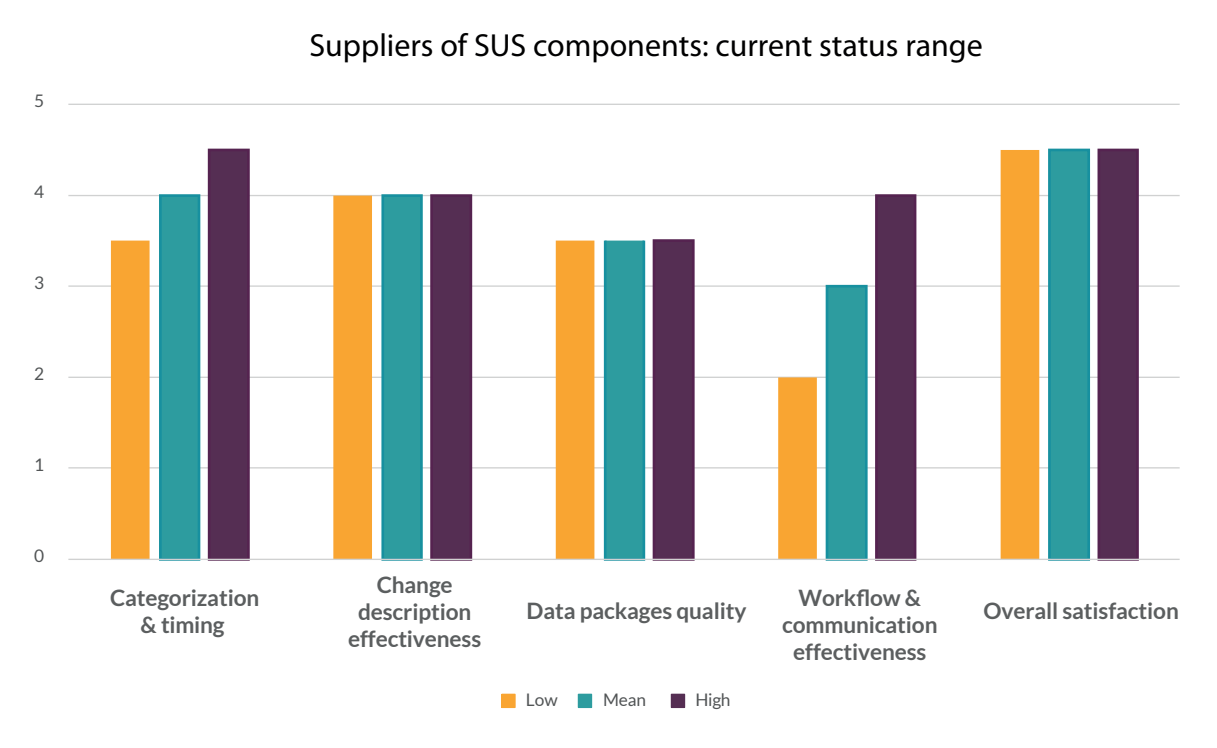


Figure 10 shows good alignment between suppliers of SUS components, however, it must be remembered that this is based on small sample size (n=2).

5.3.6 Ranking of perceived challenge and perceived impact

In the final aspect, survey respondents were asked to rank how challenging and impactful they believed each aspect of the change-notification process to be. When interpreting data, it is important to remember that the number respondents is relatively small, especially for suppliers of SUS components. Figure 11 shows how challenging companies perceived it to be to make improvements in each area.

Figure 11: Average perception of challenge of improving each area of the change-notification process

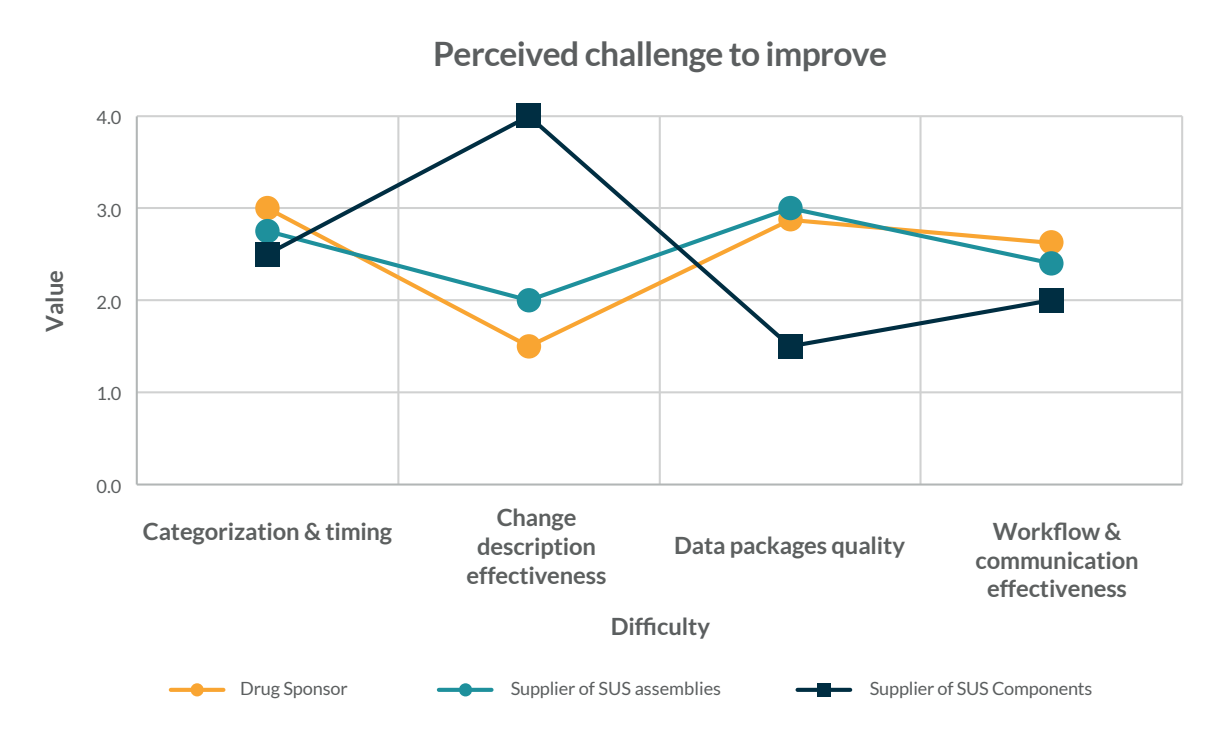


Figure 12: Average perception of impact of improving each area of the change-notification process

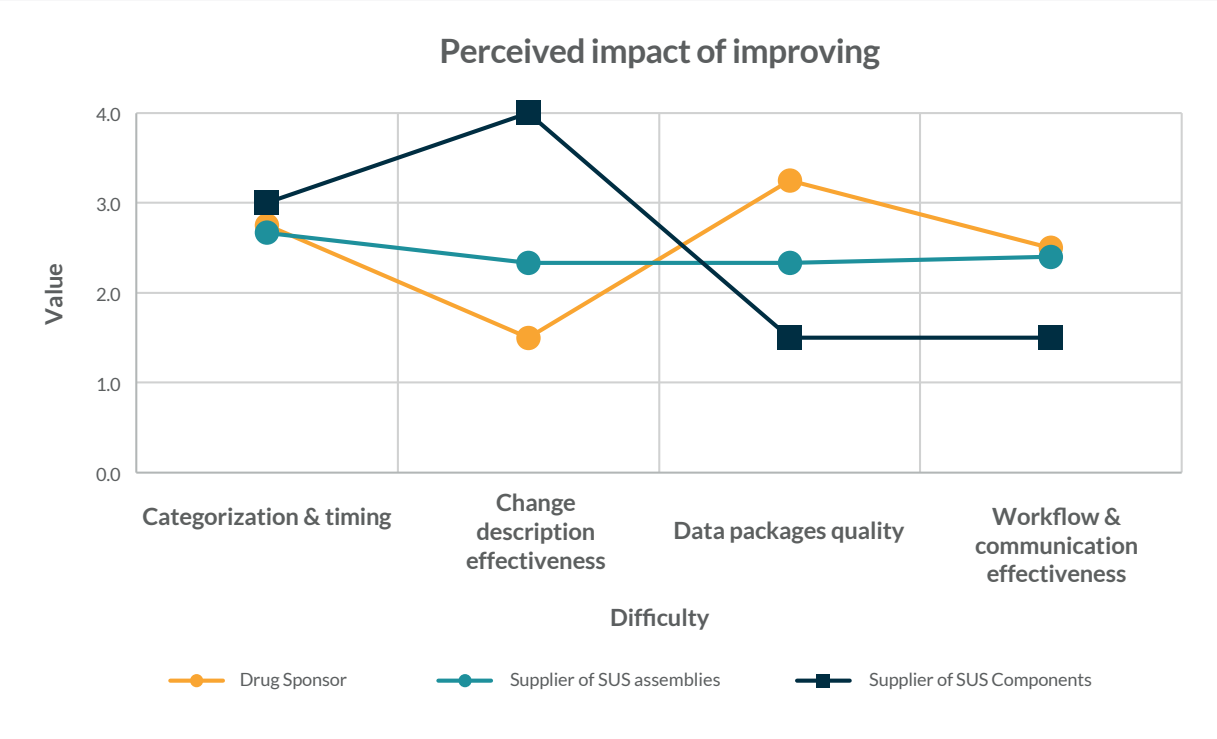


Figure 12 shows responses to the question 'How impactful do you believe improvements to each aspect of change-notification practice would be?' Effectively, the aim of these questions was to identify areas which might be both easy and impactful to address.

6.0

Discussion

The survey proved to be very useful in revealing differences in how change notifications are handled between companies throughout the biopharmaceutical supply chain.

6.1 Number of changes handled

There are clear differences in the number of changes handled by drug sponsors. This may reflect the different sizes of the organizations surveyed, or their current level of investment in single-use technologies, however all respondents were major biopharmaceutical companies. Similarly, there are differences in the number of changes reported by single-use equipment manufacturers. Size of company probably plays a role in the numbers reported by supply partners, but there is still a three-fold difference between the larger suppliers (Figure 4).

It is possible that the timing of the survey accounts for these differences, but it seems unlikely that a three-fold difference in the number of changes reported would be caused by external events alone. Such differences in the numbers of changes handled indicate a need to harmonize on the appropriate level of change reporting to avoid over- or under-notification of changes to single-use systems.

6.2 Estimation of qualitative aspects of single-use system change notifications

The team was very keen to understand what was working well and which areas offered most opportunity for improvement and asked companies to rate different aspects of the change-notification process, as their company was experiencing it overall across the industry.

Figure 5 shows the global responses, which show the system is performing moderately well across the industry, with a typical score of 3. Referring to the scorecard framework in appendix 1 (as respondents were asked to), this translates to change categorization and timing, change description and workflow and communication effectiveness being correct/effective around 50–75% of the time, as shown in Table 1. Mean scores for data package quality indicate that across the industry data packages are provided with minor gaps. This global view does not however tell the whole story with end-users typically less satisfied in most areas than supply partners. Perhaps most notably, the average score for data package quality declines from 3.2 to 2.6 when only drug sponsors are considered. As the final customer in this chain, this is critically important, especially when the scorecard-model outcome is considered which at scores of 2 indicates that there are major gaps in data packages that frequently impact implementation.

Table 1: Industry mean score for each aspect and associated outcome from the scorecard model

	Industry mean score	Level 3: maturing
Categorization and timing	3.4	50–75% of changes are categorized correctly according to the industry standard.
Change description effectiveness	3.5	A change description is provided that will allow the EU to complete the RFT IA 50–75% of the time. There may be a minor number of follow-up required to obtain proper descriptions.
Data package quality	3.2	Data package is provided with minor gaps that are easily addressed without impacting on timelines for implementation.
Workflow and communication effectiveness	3.2	Notification (and when applicable pre-notification) are provided with sufficient time to properly implement 50–75% of the time. Implementation timelines are acceptable 50% of the time or more. SPOCs are used and there is opportunity for timely and effective bidirectional feedback 50–75% of the time.

In the subsequent analysis we will look at each aspect for which a qualitative measure was requested and discuss differences between drug sponsor, supplier of SUS assemblies, and supplier of SUS component groups. We will also look at differences within the drug sponsor and supplier of SUS assemblies. We will not do this for component manufacturers as the number of respondents was low (n=2).

6.3 Categorization and timing

Categorization and timing received an average score above 3 from drug sponsors, suppliers of SUS assemblies, and SUS component manufacturers (Figure 8, Figure 9, Figure 10). Scoring was also relatively consistent within groups. This is one of the areas in which the team has focused most, so it is good to see good consistency of scoring in relation to categorization. It is surprising that the overall average score is slightly lower than for change description effectiveness, but this may reflect the lack of previous guidance/systems for the classification of changes.

6.4 Change description effectiveness

Mean scores for change description effectiveness were also reasonably consistent between different tiers of the supply chain, with average scores above 3 in all cases. There was good agreement within the supplier of SUS assemblies group on the current position, but slightly more variability within the drug sponsor group. This probably reflects the fact that the drug sponsor group were asked to respond on the basis of the changes they receive while the suppliers of SUS assemblies were responding on the basis of the changes they issue. Effectively, it is almost certainly easier for the authoring party to understand the description of a change than it is for the receiving party as the change issuer is likely to have more background information about the process and the change itself. There is an opportunity to improve change communication by digging into how effective the change description is in the absence of context about the process or detail that the supply partner holds about the change. At present, this aspect is relatively aligned, but it may need to be considered in future as an improvement target.

6.5 Data package quality

Data package quality was identified as the major area of focus for the team through 2018. As highlighted previously, this was, in part, due to the mean score of the drug sponsor group indicating that typically there are major gaps in the data packages received leading to delays in implementation and the need to request additional information (Figure 6). The team had identified high-quality data packages as an area that needed focus and would ultimately drive benefits in workflow effectiveness. What was interesting however, was the discrepancy in scoring within the end-user group (Figure 8). This led the team to ask the question, have we (as drug sponsors) defined what 'good' or 'high-quality' looks like with regard to data packages? In turn, this has led to a significant effort between supply partners and end-users to define what elements should typically be considered for inclusion in a data package for each type of change identified previously by the workstream in the 2018 paper *A guide to the classification of changes to single-use biomanufacturing systems* the categorization paper. It is expected that outputs from this work will be made available in Q2 2019. It is encouraging that this is an area the team had previously identified as significant, but for which a solution had not yet been developed. The significantly lower scores (particularly among drug sponsors) compared to change categorisation do indicate that in areas where the team has focused significant energy (change categorisation) it has been possible to improve the overall performance of the industry. Once published it will be exciting to see what impact defining 'good' data packages has on this metric.

6.6 Workflow and communication effectiveness

Perception of workflow and communication effectiveness across the industry is relatively consistent between all groups, with an average score close to 3 in all cases. This is reflective of the fact that roughly 50% of the time communication is considered effective, with correct timelines attributed to both notification and implementation of the change. The ambition of the industry is to move towards achieving effective communication 90% of the time. There is some discrepancy in scoring within the supplier of SUS assemblies group (Figure 9) and even more so within the drug sponsor group (Figure 10). The discrepancy within the drug sponsor group appears to be of roughly the same magnitude as for data packages, and it is possible that this difference in view of what constitutes a high-quality data package may also be impacting workflow effectiveness. Current thinking is that improving data

package quality will make a substantial contribution to improving workflow effectiveness. Two other aspects of workflow effectiveness that need to be considered are the use of a single point of contact and particularly the feedback mechanism by which suppliers are notified of acceptance of the change. It is important to remember that ineffective workflows can adversely impact suppliers of SUS equipment as significantly or possibly even more so than drug sponsors. As demand for SUS equipment grows, capacity and supply chain planning becomes important. If drug sponsors don't close the loop and indicate acceptance of a change it can pose challenges to SUS suppliers, in extreme cases meaning that bringing a new facility online may be delayed. In turn this may put pressure on existing facilities, potentially creating backorder situations and ultimately posing drug sponsors challenges in supplying therapeutics to market. Effectively these are challenges to business continuity planning posed by bringing new products into a regulated environment, This may be one reason why SUS suppliers on average score workflow effectiveness less highly than drug sponsors.

6.7 Ranking of the challenge and impact posed by increasing scoring in each aspect of the change-notification process

First Respondents were first asked to rank how challenging they perceived improving each aspect of the change-notification process to be (Figure 11). The first observation is that even within respondent groups there is limited agreement as to which aspect it would be most challenging to improve. If all scores were distributed equally each aspect would be ranked at 2.5. More deviation is seen from this starting point among the suppliers of SUS components, primarily driven by the small sample size (n=2). There is some indication that in general, improving data package quality and categorisation and timing are seen as slightly more challenging aspects. Change description effectiveness is generally seen as less challenging to improve by drug sponsors and suppliers of SUS assemblies. Wheras, although the sample size is small, there is strong agreement among suppliers of SUS components that the change description effectiveness aspect is particularly challenging. It is essential to collect data from a larger sample size before drawing any firm conclusions, but there are some early indications that different challenges may be faced by different tiers of the supply chain. It underlines the criticality of continuing to build understanding and rapport through the supply chain so that solutions implemented by tier 2 suppliers lower in the supply chain, ultimately address the challenges faced by the drug sponsors. Conversely, drug sponsors and SUS assemblers have a role to play in understanding the challenges faced by lower tiers of the supply chain, entering into dialogue with them, and developing solutions that work for all tiers of the supply chain.

Considering how impactful improving each aspect of the change-notification process might be (Figure 12) some trends begin to emerge. Generally, SUS assembly manufacturers consider all aspects to be equally impactful. This may be indicative of the different challenges faced by different respondents and it will be interesting to see how this evolves, as further tools and guidance are published and implemented. Interestingly, there is an inverse trend in how different tiers of the supply chain rank particular aspects. Data package quality is ranked as most impactful by drug sponsors with the impact ranking decreasing through the supply chain. Conversely change description effectiveness is seen as least impactful by the drug sponsors and the impact ranking rises through the supply chain. This may indicate that drug sponsors rely heavily on critical analysis of the data provided to support a change and less on the description of the change provided by the supplier. This data-driven approach taken by drug sponsors is wholly consistent with operation in a regulated environment. Change description effectiveness may however have a key role to play in setting the context of the change or in providing better understanding of the technical aspects of supplier manufacturing processes with which drug sponsors may not be familiar. This may be why SUS component manufacturers have scored this highly.

7.0

Conclusion

Performing this survey has been a very useful exercise, providing some great insights into current areas of convergence and divergence of companies' experiences with change-notification process throughout the biopharmaceutical supply chain. Importantly, since this is the first time the survey has been run it has established a baseline in terms of current performance of the change-notification processes employed by respondent companies. It has highlighted significant differences in the number of change notifications drug sponsors are handling for single-use systems. Establishing the current status of these practices is important as the intention of the team is not to increase the number of change notifications received, but rather to identify and focus on the change notifications likely to have the most impact.

The survey has also been very useful in uncovering a 'revealed problem'. End-users consider data packages to be highly impactful to the change-notification process. A good data package, delivered with the change notification, provides the leanest workflow and minimizes the need to follow up with additional questions to the supplier. Since the drug sponsors are the ultimate customers in this supply chain, they will typically drive rework and requests for additional information from the supply chain. Figure 8 shows that there is a lack of agreement between drug sponsor companies on the quality of the data packages they currently receive. Reflecting on this, the team acknowledged that at the time of the survey, little work had been carried out to define what constitutes 'good' with respect to single-use system change-notification data packages. Without alignment between drug sponsors it is very difficult for supply partners to meet expectations as these may differ between drug sponsor companies. The impact of this on timelines may be exacerbated when requests for additional data need to be passed on from tier 1 suppliers through the supply chain. Team agreed to a subgroup composed of both drug sponsors and suppliers working todevelop guidance on data package recommendations.

Moving forward, the survey has allowed companies participating in the BioPhorum initiative to measure the current status of key aspects of the change-notification process that their best practice is intended to address. This forms a baseline against which continuous improvement efforts can be measured. A key revealed problem has been identified prompting the group to develop content to address this. The intention is now to run this survey with a broader audience and continue to measure the impact that our best-practice proposal is having on change-notification single-use systems within the bioprocessing industry. As more companies implement this practice, when this survey is repeated it will be possible to measure whether the goals of the collaboration (>90% right-first-time change notifications) are being met or whether there is a need to correct the course by adapting ways of working or revising published tools and guidance.

Appendix

BioPhorum BPSA Change Notification Scorecard Framework

Attribute	0	1	2	3	4	5
Categorization and timing	BioPhorum or other industry standards (ASTM, USP, etc.) to assign change categories are not used.	Less than 25% of changes are categorized correctly according to the industry standard.	25–50% of changes are categorized correctly according to the industry standard.	50–75% of changes are categorized correctly according to the industry standard.	75–90% are categorized correctly according to the industry standard.	At least 90% are categorized correctly according to the industry standard.
Change description effectiveness (and anticipated end user (EU) impact assessment (IA))	A description of the change is not provided or the description provided does not allow an EU IA. There may be a significant amount of follow-up required to obtain proper descriptions.	A change description is provided that will allow the EU to complete the right-first-time (RFT) IA less than 25% of the time. There may be a significant amount of follow-up required to obtain proper descriptions.	A change description is provided that will allow the EU to complete the RFT IA 25–50% of the time. There may be a significant amount of follow-up required to obtain proper descriptions.	A change description is provided that will allow the EU to complete the RFT IA 50–75% of the time. There may be a minor number of follow-up required to obtain proper descriptions.	A change description is provided that will allow the EU to complete the RFT IA at least 75–90% of the time.	The change description provides sufficient information to allow the EU to complete the RFT IA at least 90% of the time.
Data package quality	Data packages are not sent with the change notification, and data is not available.	Data package is provided but with major gaps and rework is required, impacting significantly on timelines for implementation.	Data package is provided with significant gaps and rework is required, impacting on timelines for implementation.	Data package is provided with minor gaps that are easily addressed without impacting on timelines for implementation.	Data is available with no gaps but it is not always sent with the notification and must be requested.	Data is always available, with no gaps and sent with the notification (right first time).
Workflow/ communication effectiveness	Pre-notification is not provided (when needed). The quality and timing of the notification is not acceptable. Timelines for change implementation are not acceptable most of the time. SPOCs are not used. There is no opportunity for bidirectional feedback.	Notification (and when applicable pre-notification) is provided with sufficient time to properly implement less than 25% of the time. Implementation timelines are acceptable less than 25% of the time. SPOCs are not used. There is opportunity for timely and effective bidirectional feedback less than 25% of the time.	Notification (and when applicable pre-notification) are provided with sufficient time to properly implement less than 25–50% of the time. Implementation timelines are acceptable 25% of the time or more. SPOCs are used and there is opportunity for effective bidirectional feedback 25– 50% of the time.	Notification (and when applicable pre-notification) are provided with sufficient time to properly implement 50–75% of the time. Implementation timelines are acceptable 50% of the time or more. SPOCs are used and there is opportunity for timely and effective bidirectional feedback 50–75% of the time.	Notification (and when applicable pre-notification) are provided, with sufficient time to properly implement, 75–95% of the time. Implementation timelines are acceptable 75% of the time or more. SPOCs are used and have timely and effective bidirectional feedback 75–90% of the time.	Pre-notification (when applicable) and notification are provided, with sufficient time to properly implement, at least 90% of the time. Implementation timelines are acceptable 90% of the time or more. SPOCs are used and have timely and effective bidirectional feedback at least 90% of the time.

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