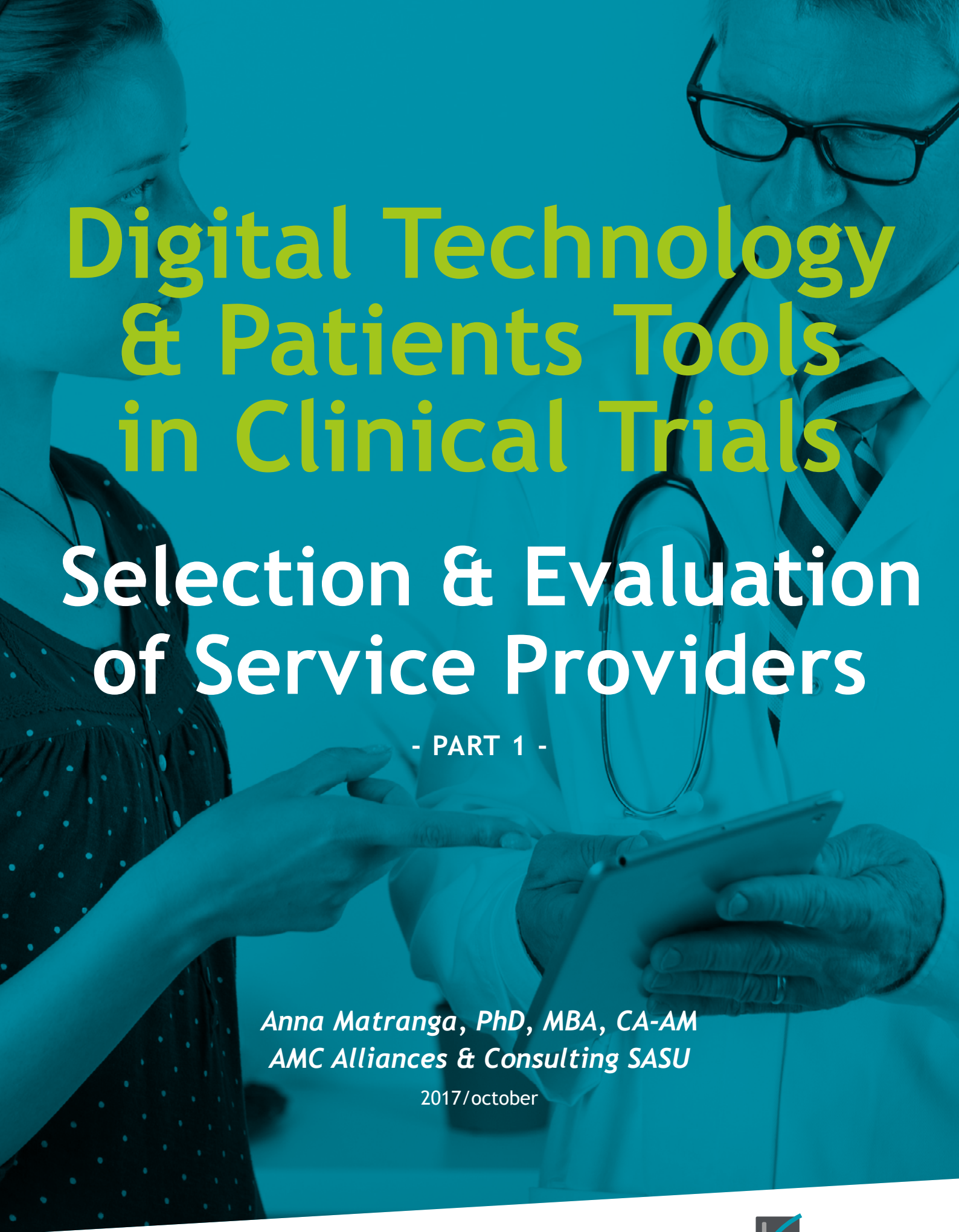

Digital Technology & Patients Tools in Clinical Trials

Selection & Evaluation of Service Providers

- PART 1 -

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Dedicated to eCOA & Patient Engagement

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Introduction

Digital technology today has become an important tool in facilitating access to and engagement with subjects participating in clinical trials. This technology is enabling the direct collection in real-time of patient data. This includes their symptoms (be it pain, vital signs, etc), overall mental state, the effects of the disease or condition on their day to day functioning (e.g. mobility, day to day quality of life) and how well or not they are progressing.

Therefore, the adoption and use of ePRO (electronic Patient Reported Outcomes)/eCOA (electronic Clinical Outcome Assessments) devices [1] as well as wearable devices such as glucometers, vital sign sensors and the Ava bracelet (plus other technologies) are facilitating:

- Improvements in data quality & in data gaps
- Improvements in patient protocol compliance
- Greater study power requiring fewer enrolled patients.

And ultimately, the improved monitoring of lifestyle evaluation/ well-being of patients both in clinical trials and beyond this into medical practice.

These advances are enabling patient access, improved follow-up in patient care & doctor/patient relationships and is intended in the long-term to facilitate the reimbursement of drugs with a "proven therapeutic value"[2][3][4].

So how do companies go about adopting this technology?

When considering all technology companies/suppliers out in the field, who to use and what technology could support the business goals, it is key to ensure firstly that the business strategy/objectives in place are clear, coherent and transparent to all in the company. Pharma companies are not (yet) technology companies (and should resist becoming one) as their goal is to develop medical therapies/ solutions for patients. It is important to underline the pecking order so that any company's digital strategy supports the overall business strategy and not vice versa.

- It is key to remember that any technology developed in-house or provided by external partners/providers (recommended approach as it's a fast-moving market, enables quicker access to technology, and cheaper too) should support company objectives across the entire business organisation rather than vice versa. Jumping on the integration bandwagon of new technology without a clear vision of where the company is heading for and what the technology will provide in terms of benefits to the business will incur major problems of undue expenditure and potential delays to business growth.

- The industry may use the language of being "data driven" but is primarily "patient-focussed", "science -focussed" with the aim of bringing value to patients and the scientific community/healthcare system in each country through the development of medical therapies/solutions.

- It's also worth remembering that you don't win/engage the interest of patients and investigators by having the best technology or wearable devices (albeit a short-term thrill) but rather by having the best treatments for their health problems.

Thus in the evaluation of more & more new technologies, the questions needing to be addressed are:

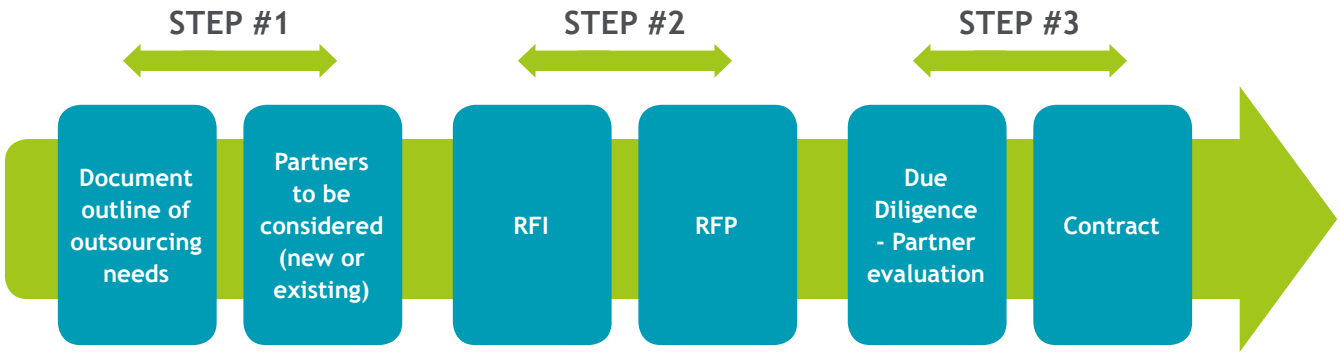
- What are the benefits/value it will bring to the business?
- What are the endpoints to select and how will the data generated from these endpoints be used?
- How do we identify/assess/ensure that the study endpoints/measures that need to be collected, make sense/are meaningful to patients? Because if they don't the patient will not take care/be conscientious in the collection process.
- On what programmes/projects should the technology/devices/wearables be used and on which should they not (little benefit)? Do we apply it to all the business or just partially? Where will it make a difference? What are the needs in terms of longterm and short-term resources/costs?
- Do we have the internal expertise (operations: scientific & IT profile) to adequately evaluate the selection of technology providers? Are there existing skills gaps that inhibit efficient delivery? Are they able to address current needs and future needs beyond 3 years or more? And if not, can we buy this (consultants/subject matter experts) and/or develop in-house as a long-term investment towards competitive advantage and sustainability?
- Do we see value creation through on-boarding, integrating and & upgrading technology solutions? Or would we rather prefer to outsource to one or multiple providers? If so, how do we ensure the correct level of oversight to make sure the risk/benefits are well-managed?

- If there is only one provider selected, how will the sponsor and provider facilitate/promote innovation in technology to support long-term business needs? If multiple providers are selected will it be feasible to manage/deal with the complexity of different relationships across different functions/projects/programmes in order to achieve harmonisation, efficiencies, value creation, transparency as well as compliance to regulatory requirements.

- And lastly, if there are several providers how does the internal IT platform/architecture support and enable integration of new technology sourced from different providers. How can the company leverage the same technology across the company in different functions or business units? And what should be the duration of the deal for programme needs mitigating the risk of potential obsolescence of the technology? Does the ROI (return on investment) calculation **justify the expenditure to make the technology 21CFR Pt 11/GCP compliant and what are the regulatory hurdles to overcome?**

This white paper attempts to structure these questions in the due diligence process (see Figure 1) for selecting and evaluating technology providers for pharma R&D. Its aim is to provide a simple and practical checklist tool (and process) that can be used by those involved.

Figure 1 - Selection & Evaluation Steps in the Choice of Service Providers



RFI = Request For Information
RFP = Request For Proposal

STEP #1

Technology Providers
Who & how to identify them?

So once the strategy is clear and there is agreement to explore the technology available from external providers, how do we identify a short or long list of providers that we want to talk to investigate/evaluate their technology & its interest/relevance to our business model?

Here are some questions on "knowing your needs" to consider:

- Does the technology address existing/future business needs?
- Has the technology been used/tested by industry peers or by other industries?
- What's is the technology company's experience in technology/devices in healthcare/life-sciences/other?
- Does the company have a product/technology roadmap and/or research & innovation department?
- What's their reputation – e.g. articles in the press on the company and/or its senior managers, speaker participation at industry conferences, known by/contacts with members of the internal team? Feedback from industry peers?
- What is the experience/seniority of their staff/personnel?
- Where to and how to find the companies? Investigate conference speakers, seminars, articles in press, word of mouth, scouting, etc.

On-boarding technology as patient tools can be a costly investment in terms of integration and long-term investment, thus it may be worth making the list a "long" shortlist…

Doing it right the first time and using the exercise to learn from the different companies and to adapt/finetune the technology requirements/implementation going forwards will be invaluable.

The screening/scouting process for technology providers can be a two-step process where:

1. **USE OF AN INTERNAL CORE TEAM** (1-3 members consisting of Clinical Dev/Operations and IT) to quickly determine via a webinar demo/presentation whether the technology is "fit for purpose" or not vis-a-vis the company's objectives. They will decide the value or not in maintaining the supplier on the list as a candidate for full evaluation/due diligence.

PS, this necessitates full transparency (with a documented, simple decision matrix containing the recommendation or not to go forward) to ensure that the screening process is respected/approved by the key company stakeholders and to avoid, wherever possible, delays/prolongation of the selection process. The nature of the fast developing apps/technology may be such that it is difficult to avoid new suppliers to the shortlist (in the continuous process - evaluate, pilot, use, re-evaluate, develop or replace) …Bring on-board the legal team/function here so that when the technology provider comes with their CDA prior to demo, the contract can be signed quickly and there is no legal bottleneck (unaware & unavailable), due to lack of/limited resources, to support this.

Then…

2. **OPERATIONS/IT:** Once your list is final, ask all companies shortlisted to provide information on their company and its activities via an RFI (request for information).

In the case, where you are comparing similar technologies and wish to compare costs upfront, it is advisable to obtain a RFP (request for proposal) to get a costing of the technology for implementation/ integration. If reviewing different technologies, a ball park estimate should be adequate at this stage of the process.

OPERATIONS/LEGAL: Contractually, it is worthwhile sending a confidentiality agreement as well as a draft master services/technology agreement to be shared with the legal teams upfront to initiate the review process as soon as possible avoiding operational delays due to a potential legal department bottleneck once the choice of the technology provider has been made. If an MSA is not available internally, ask the provider for one & review with legal/IP departments.

QA: At this point, it's also of value to consult your QA representative to identify future dates for an audit of the technology, processes and people. This date can be shared with your shortlist candidates so that they are available/accessible should they be chosen from the shortlist.

FINANCE/PROCUREMENT: Initiate the review process to determine the financial stability of companies on the list. Conduct a market intelligence survey to identify what is in the press, being said about these companies & their senior management e.g. activity, partnerships/mergers, articles on key employees, recent awards/announcements.

NETWORK: Last but not least – what is the link with senior management of your suppliers? Is there already an established link that will help you in future to quickly resolve issues/resourcing? An important matter to consider when implementing the governance structure (*NB. to be covered in a second white paper*) at a later date as well as being one of the key selection criteria in your matrix. The senior contact between companies is truly beneficial if it occurs at an early stage of the process.

Once this process is initiated, it is worth its integration into the company culture/processes as a principle of "continuous due-diligence" whereby dedicated (competent) resource promotes the ongoing scouting of "state of the art" technology to leverage the business strategy/objectives. There are many start-up/small technology companies on the market thus some pharma companies have put this scouting function into their business development/licensing team as part of their strategic direction while others still in the exploratory phase have created tech innovation managers within the function e.g. R&D/Other department.

STEP #2

Due diligence/evaluation process of providers Request for (What) information?

The evaluation process requires a multi-functional team of key stakeholders.

- **Key stakeholders/functions in the evaluation process** should include: clinical managers, data scientists, bioinformatics biostatistics, medical/PV, Technology/IT representative, procurement/outsourcing, finance, QA, regulatory & legal affairs. A leader of the process should be assigned to coordinate the progress/status to senior management. It is also important that each member of the team is sufficiently experienced to conduct an effective evaluation within the time limits assigned to do so. The extent of involvement will be dependent on the individual responsibilities outlined upfront (e.g. finance may not need to be present at meetings/demo's but nevertheless should be copied in on all project/progress communication)

- **Is the technology to be used by R&D alone** or by medical affairs and/or commercial operations and/or other departments too? This should be established upfront to enable all key players to be included in the evaluation process. And do some members have a greater say in the final choice? Get clarity on this. Organising a meeting to clarify this process and to underline the expectations of senior management will ensure transparent project team objectives. In addition, if this technology is key in fulfilling the company objectives then senior managers need to be present/actively involved to demonstrate the commitment to the implementation/integration of this new technology as well as providing support on project team

focus/objectives. It's important that the team agrees on what its looking for/objectives as well as the scope of the due diligence – who is responsible for what part of the evaluation. Additionally, the team should determine an objective evaluation system with key categories and an associated rating system.

- **The evaluation criteria** should be determined and agreed upon with an "objective" scoring system/rating (eg. 0= doesn't meet needs, 1=meets needs, 2=exceeds needs). Each function may have a greater/lesser influence when it comes to rating the different criteria e.g. the scoring of the technology usability for the clinical trial may be higher/more important when rated by the clinical and IT team in contrast to the scoring of the organisational/business information criteria which may be more important to procurement/outsourcing/finance functions. In addition, service specific criteria may have a higher weighting when service duration is limited to 3-6months whereas business/financial stability of the company can become equally important if the service duration is from 1-5years.

Evaluation criteria may be broken down into three categories:

- Organisational/Business Information
- Service-Specific Capabilities - Technical/Scientific
- Other – Regulatory, Compliance, Research, etc

Within these categories, identify/define upfront the potential "show stoppers", what will kill the deal to avoid the resource utilisation (& cost) on technology/company that doesn't fit with objectives.

CHECKLIST

ORGANISATIONAL/BUSINESS INFORMATION

Criteria to be considered (not an exclusive list) are:

Financial health (indicators of profitability, solvency, funding, etc.)
Repeat business with a solid backlog of projects/contracts
Organogram/Culture - clear roles and responsibilities, decision-makers, management team, CEO/CIO profiles
Resourcing - infrastructure for project team support & back-up (across geographic cover/ technical) Staff location/turnover/profile- Seniority in the company/role Ratio of senior/experienced staff to junior/less experienced staff Duration of senior managers in the industry
Evidence based experience - the company/individuals have established R&D IT experience
Potential business volume with this CRO i.e. Sponsor's importance to CRO
Financial stability of co-devl't Providers – duration of relationships with subcontractors
Cultural Fit – "How we do things here"
Interface/Professionalism/Team Cohesion

SERVICE-SPECIFIC CAPABILITIES [5]

Criteria to be considered (not an exclusive list) are:

Product – Technology & its Usability
Demo of technology (ePRO, eCOA, wearables, sensors, apps, etc) - What are the strengths, weaknesses, opportunities, and threats (SWOT) to validate alignment with business objectives (e.g. patient engagement & data collection)
What's the satisfaction levels of users (acceptance test, usability, further development of devices)
Number of Countries and number of sites and number of patients managed -exposure/global footprint
Use & Experience in Gamification

Product/Technology Support

Helpline 24/7 - Breakage/Damage/Repair/Device inventory

Training capabilities for subjects/healthcare providers (HCPs)

Tracking the support call generators to anticipate product problems

Technical Resources

Staff Competency Level & Training Records (profile & ratio of Data scientists/Data analysts, Data/Medical reviewers etc)

Team Structure/Proposal – Seniority & Experience (In & Outside Industry)

Processes

Opportunities for efficiency gains and/or cost reduction

List of SOPs/Versions/Updates

Device Provision/Supplies - Planned schedule for device delivery? Back-Up Plan

Disaster recovery plan (incl. meteorological disruption)

Processes for data storage, review, trends/outlier identification, Just-In-Time validation, scale-up, issue & audit log management

Project Procedures: project plan, Communication / Escalation plan, risk & issue management

Performance Issues? Existing procedure on what to do?

Performance/ KPIs for service monitoring/delivery

Architecture - Systems/Validation

Compatibility/Ease of technology integration with Internal IT architecture/core platform

Cloud/Data hosting

Warehouse facilities/Data capacity management/Long-term storage

Validation systems eg. 21CFR pt 11

OTHER CAPABILITIES/CRITERIA : REGULATORY, COMPLIANCE, RESEARCH

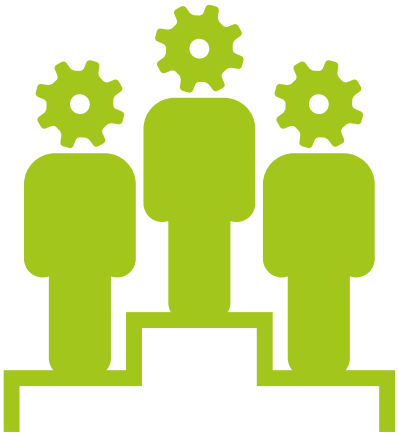
Regulatory, Compliance
Internal & External Audits/Regulatory Inspections – Reports/Findings/Recommendations
Regulatory requirements/GCP compliance (incl. data protection, ICH6R2, cyber security)
Records of discussions with regulatory authorities
Technology – freedom to operate – can be used without infringing third party patents

Research/Innovation
Dedicated Research Team?
Innovation/Future projects (eg. devices/apps)
Pilot studies/methodology/ Implementation Phase
Technology/Product Roadmap (long-term business value)

Look for reasons to kill the deal!
Define the potential showstoppers, eg.

- Financial problems
- High staff turnover
- Little exposure/use of technology

STEP #3



Due diligence – Selection of provider(s) of choice

- Conduct a meeting with all key stakeholders to evaluate/compare the strengths/weaknesses and opportunities/threats (SWOT) of each company and their technology - have you already eliminated the show stoppers? And if not, why not (documented rationale)?
- Does the demo confirm the importance of the technology vis-à-vis the company objectives?
- Who? Which companies and which technology have the highest scores from the due diligence/evaluation of Service-Specific Capabilities? This requires discussion across the team to get agreement on this.
- Interface/team players - In F2F meetings/webinars for evaluation, how does the team come across? Are they professional in their management of questions? Do they act as a cohesive team? Do they demonstrate their knowledge/proven experience with the targeted technology? Are they using/talking the same language, is the dialogue clear and it's easy to get the message across, would it be easy to work with them? is there a connect/chemistry between the different functions of each company?
- Based on the outcome of this meeting (shortlist of 1-3 Providers), obtain further information concerning the business aspects eg. credit ratings of SPs, list of additional questions/issues that need to go back for further clarification to the provider, if not done already, obtain a cost proposal from RFP (one-off study cost/programme, cost of piloting/on-boarding the technology).

- Identify the need with the QA department (documented risk assessment and corresponding recommendation) for a pre-contract audit or an audit to be planned after project start.
- Based on the overall evaluation rating, feedback on questions/ issues, credit reports, cost, annual reports/press releases/ industry analyst or consulting reports and any available references, make a team decision on the choice of the preferred provider(s), document appropriately and get sign off by the team/key stakeholders and by senior management.
- This final decision should be endorsed/pending the pre-contract audit, if deemed necessary (audit – access to relevant staff, documents, data?).
- Once done the decision is communicated to the selected provider(s) and the unsuccessful provider(s) is/are informed.
- Then the operational planning/kick off meeting, contract process and governance/oversight may be initiated.

In Summary

It's important to ensure that in Due Diligence/Selection:

- The chosen technology(ies) support(s) the business strategy and enables investigator site and patient engagement,
- The availability (internally or externally) of data analytic capabilities to support the future positioning of the therapeutic value, personalised medicines and reimbursement potential,
- There is senior management commitment and support of the team decision.

Implementation/ Integration should identify whether:

- The technology is R&D or companywide and if there is compatibility with internal IT platform architecture/systems
- There are adequate skilled IT resources & engagement for the duration of the technology use (be it short-term or long-term)
- The frequency of training/lessons learned sessions to on-board the technology and **streamline/adapt internal process for all key team members**

A theme causing much discussion at industry conferences of late is the urgent need to develop (and "how") the competencies in data science, informatics, business intelligence and alternative statistical approaches to manage this influx of technologies as a new business model for drug development. It is a critical need in the management of the mountains of data being collected. Thus, with the entry of new CIOs into the industry [6] and/or the increasing visibility of the CIO role e.g. innovation awards in this field [7], there will hopefully be a strategy on how to bring in/develop this competency in order to "evolutionise" the business model towards sustainable business growth. It is clear that the drug development world is moving faster and faster and that the industry needs to identify & embrace the new ways of doing things as well as engage regulators with it.

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