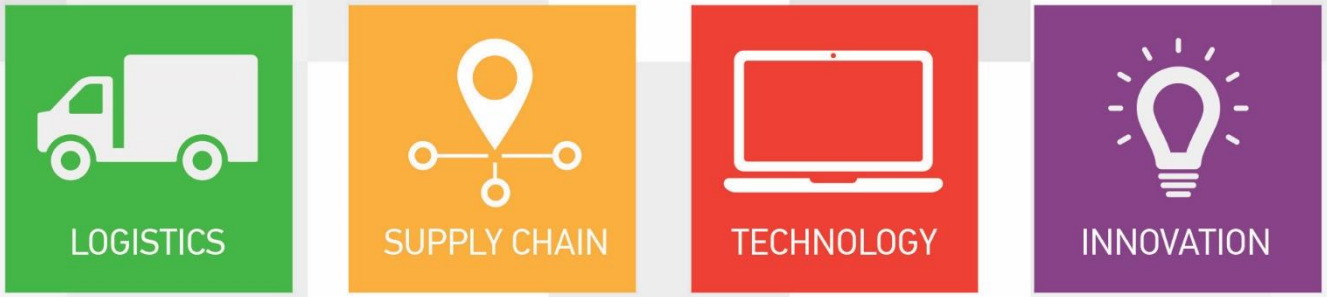

ASSESSING THE CURRENT AND FUTURE STATE OF CLINICAL TRIAL SUPPLIES

ARENA INTERNATIONAL EVENTS GROUP

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1. EXECUTIVE SUMMARY

The average cost to develop a drug is $2.6 billion and one major component of that spend is within the clinical supply chain. As the investment in the biotech and pharmaceutical industry is only increasing, the importance of running an efficient and productive supply chain also increases.

In order to gain a deeper understanding of this rapidly evolving Clinical Trial Supply market, Sonoco ThermoSafe, Berlinger & Co. AG and Arena International Events Group conducted a comprehensive and forward looking survey across global regions. The survey was co-developed by an advisory panel of leading industry experts from AstraZeneca, Clinical Supplies Management, FibroGen, GlaxoSmithKline, OPKO Biologics, PCI Clinical Services, QuickStat Global Life Science Logistics and Sunovion Pharmaceuticals.

The survey consisted of five sections: respondent demographics, logistics, technology, supply challenges and innovation. 230 individuals from the clinical trials community completed the survey, with the vast majority based in the United States, with annual company revenues below $250m or above $1Bn. Half of the respondents were involved in drug development, with the remainder involved in clinical trial supply services (e.g. drug sourcing, packaging and distribution).

The survey reveals a number of strong trends shaping the future of clinical trial supply:

- Growth in the adoption of Direct-To-Patient distribution model, driven by the desire to optimise cost of recruitment, patient interactions and leverage efficiencies in data collection/visibility using technology and specialist service providers.
- Accurate and proactive supply forecasting is heavily influenced by the partnerships between clinical and operational teams. In particular, supply chain collaborations with the ability to integrate data and tools with CRO, CMO, distributors and packaging suppliers.
- Technology has the potential to reduce some of the supply chain issues highlighted in the survey. Wider adoption of technology can be achieved if vendors make solutions that address data security, easier mobile user interfaces and ability to integrate with existing systems.

This report provides an analysis of the survey results, examining the current situation and exploring the future opportunities and challenges for the global clinical trials supplies market. Additional insights from the Advisory Panel have been incorporated to broaden the perspective and stimulate a wider industry debate.

The survey data, commentary, analysis and opinions in this publication are those of the individuals themselves and do not reflect those of their organizations and/or its personnel.

The complete results and analysis of the survey will be formally presented publicly throughout 2017 at Arena International Events.

2. SURVEY PROCESS AND METHODOLOGY

The survey commenced on March 1, 2016 and ended on December 31, 2016. It was conducted using Survey Gizmo, an online survey creation, tracking, and analysis tool. The survey consisted of 33 questions with a comments section included for specific questions. None of the questions were mandatory and therefore, partial surveys were submitted and accepted. Promotion of the survey was done with the support of various internal resources and external partners.

- Sonoco ThermoSafe website and newsletters
- Arena International Events Group website and email newsletters
- Berlinger & Co. AG website and newsletters
- Sonoco ThermoSafe direct customer contact through email and in-person visits
- Promotion at Arena International Events Group industry conferences
- Pharmaceutical Commerce website and email newsletters
- Healthcare Packaging website and email newsletters
- Pharmaceutical Online website and email newsletters

The survey consisted of 4 sections, covering a range of topics from logistics and supply challenges to innovation and technology.

There were various question types including:

Multiple choice – select one

For this type of question, the respondents were asked to select one answer from a list of possible options. The number of responses received for each option was divided by the total number of respondents that answered the question to achieve a percentage. All responses add up to 100%.

Multiple choice – select multiple

For this type of question, the respondents had the option to select multiple answers from a list of possible options. The number of responses received for each option was divided by the total number of respondents that answered the question to achieve a percentage. Hence, all responses do not add up to 100%.

Ranking

For this type of question, the respondents were asked to rank the top three out of a list of possible options. The total score for each option is a weighted calculation. Items ranked first are valued higher than the following ranks.

3. SURVEY RESULTS

3.1 Participant Demographics

76% of responses were from organizations based in North America, with 12% from Europe and 11% from Asia (Fig. 1). These organizations were conducting business across the globe with 26% in North America, 23% in Europe, 20% in Asia with the remaining responses for South & Central America (Fig. 2).

Over half of the responses were professionals from pharmaceutical/biotech organizations. 17% were involved in packaging or logistics, while 14% worked for Contract Research Organizations (CRO) and related clinical support services (Fig. 3).

Fig. 1: Survey respondents by region

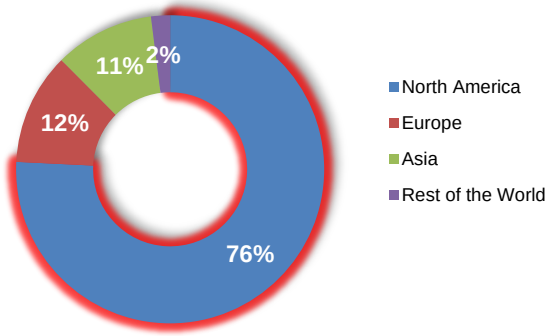


Fig. 2: Regions where you do business

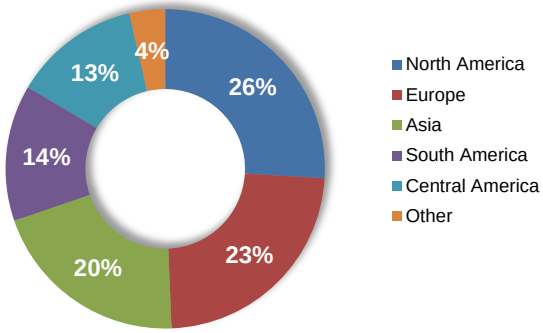
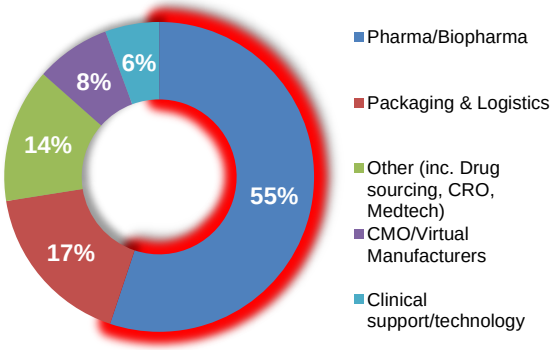


Fig. 3: Survey respondents by industry



Half of survey participants worked for organizations with annual revenues above $1Bn, followed by a quarter with annual revenues below $50m (Fig. 4).

Fig. 4: Survey respondents by company size
(Results filtered: Sponsors only)

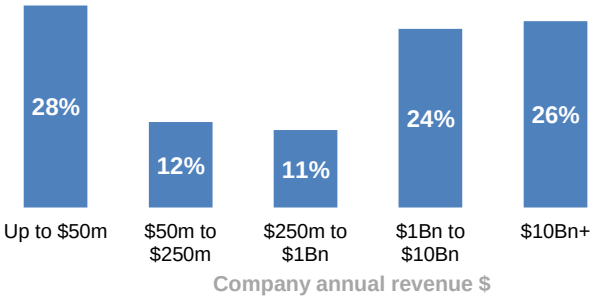
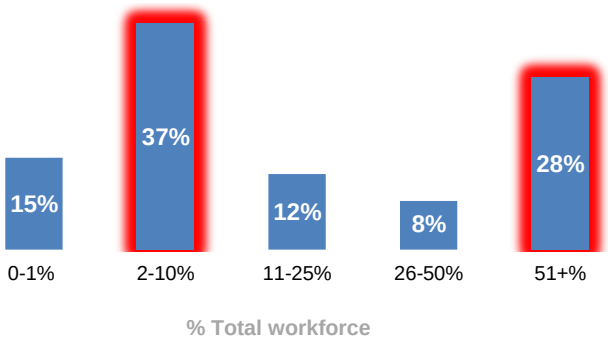
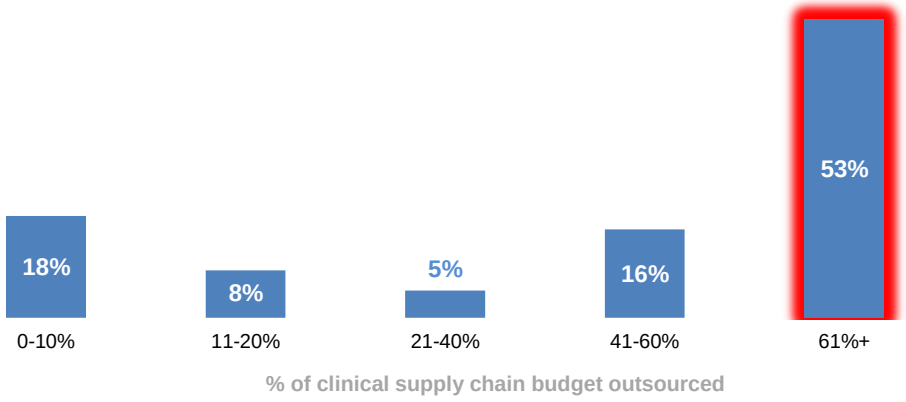


Fig. 5: Staff dedicated to clinical supply activities
(Results filtered: Sponsors only)



The survey asked participants how much of their clinical supply budget was outsourced, with around three quarters citing some degree of outsourcing and two thirds outsourcing at least half of their budget (Fig. 6).

Fig. 6: % of respondants who outsource aspects of clinical supply
(Results filtered: Sponsors only)



Advisory Panel Insight

- *While API and DP may still be largely in-sourced within Pharma, finished goods production is largely outsourced. I remember someone gave a talk over a decade ago predicting that supply chains will one day become entirely outsourced, many companies are already there and we all are steadily moving that direction.* *(Catherine Hall, Director of Operational Excellence, Sunovion Pharma)*
- *We are seeing a continued trend toward outsourcing clinical supplies. We recently hired an entire team from a large Pharma that went to a full outsourced model. We also see companies with in-house capabilities outsourcing unique needs.* *(Bob Albanese, Senior Vice President, Clinical Supplies Management)*
- *We are seeing a steady migration from a tactical, project based outsourcing model to more of a strategic and increasingly integrated outsourcing model. Clients are trying to reduce the amount of vendors they work with, so selection of the right partner is crucially important.*

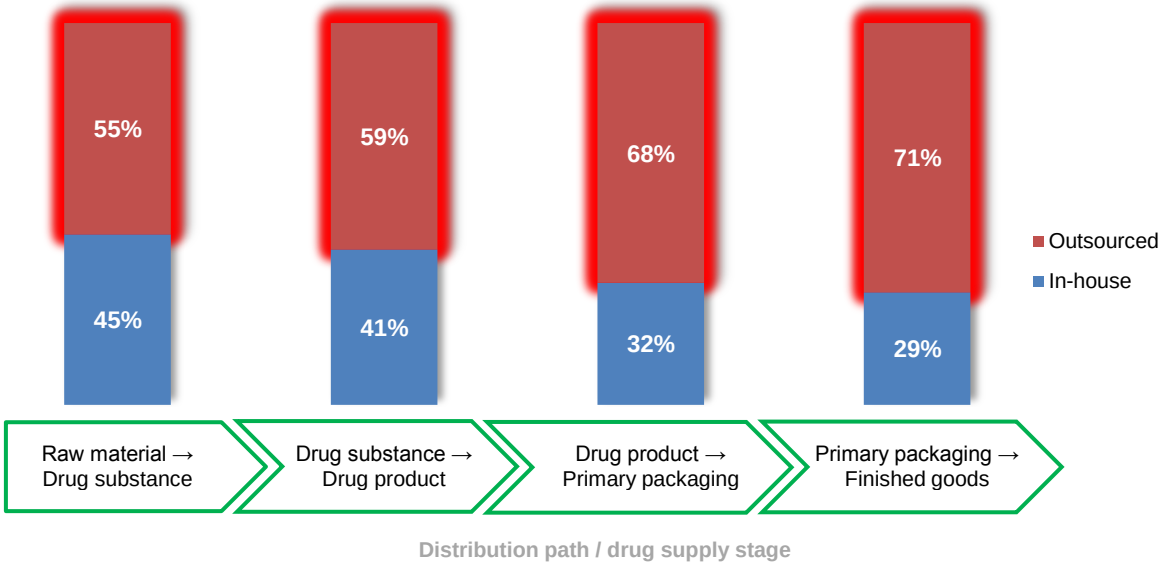
  (Brian Keesee, General Manager, US Clinical Services, PCI)

3.2 Logistics

3.2a Distribution Paths

Outsourcing of logistics occurred more frequently in the later stages of drug supply, retaining early stages more in-house (Fig. 7). 71% of respondents outsourced logistics for the primary packaging to finished goods distribution path, followed by 68% for the drug product to primary packaging path, 59% for the drug substance to drug product path and 55% for the raw material to drug substance path.

Fig. 7: Logistics method utilized by distribution path/drug supply stage

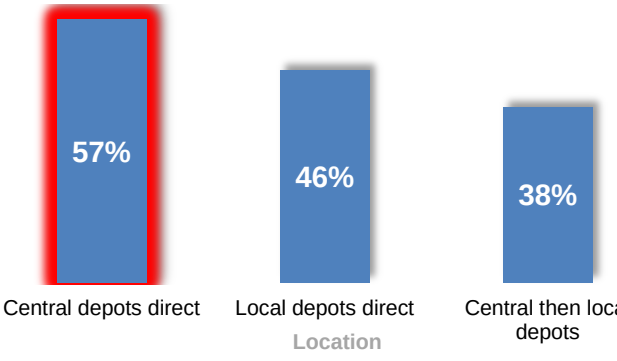


The survey asked which distribution pathways were used for finished goods, with 57% of respondents distributed directly to a central depot, followed by distribution directly to a local depot 46% and 38% distributing to a central depot and then on to a local depot.

Advisory Panel Insight

- *The variety in distribution paths remains a large challenge for clinical supply chains and continues to set them apart from commercial counter-parts. (Catherine Hall, Director of Operational Excellence, Sunovion Pharma)*
- *While this is a good representation of current or past models, we are seeing some variance when direct-to-patient (DTP) distribution is introduced which at this time is a small percentage. We expect to see the DTP model make an impact on these metrics in the future. (Bob Albanese, Senior Vice President, Clinical Supplies Management)*

Fig. 8: Distribution pathway used for finished goods

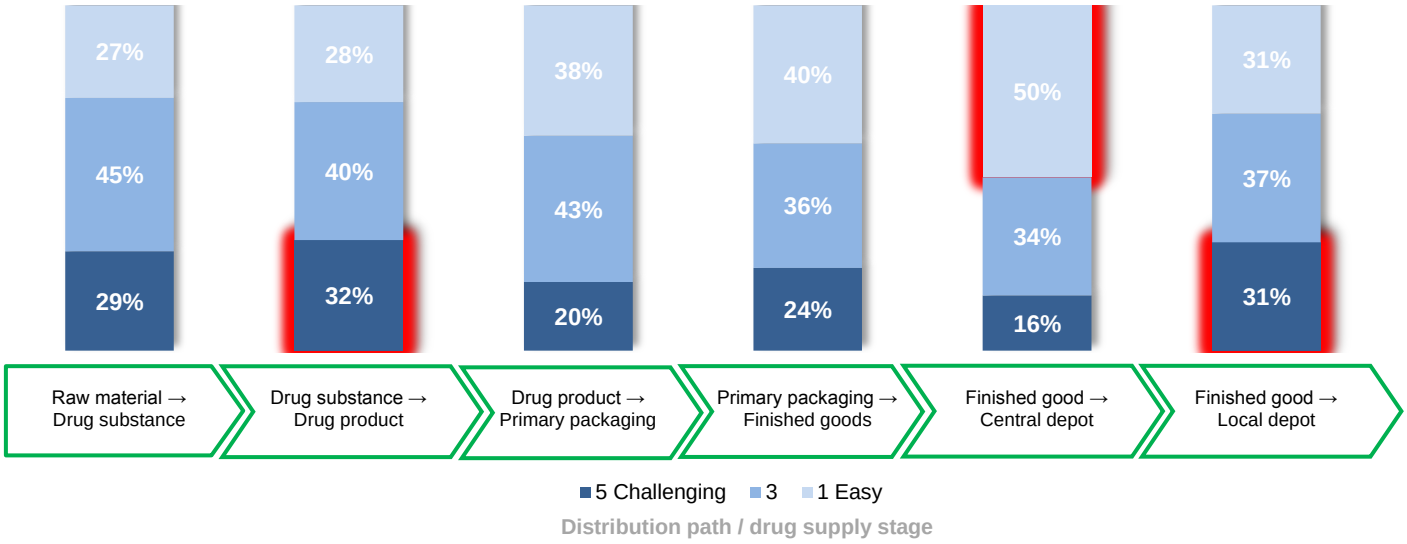


- *We do see interest and adoption of Direct-to-Patient studies, but also a more broad re-engineering of traditional supply chain models. Concepts like late stage customization, Just-in-time supply, and adding value closer to the local investigator site can be really impactful to timelines and making the study much more reactive to changes when needs arise. (Brian Keesee, General Manager, US Clinical Services, PCI)*

3.2b Logistics Challenge

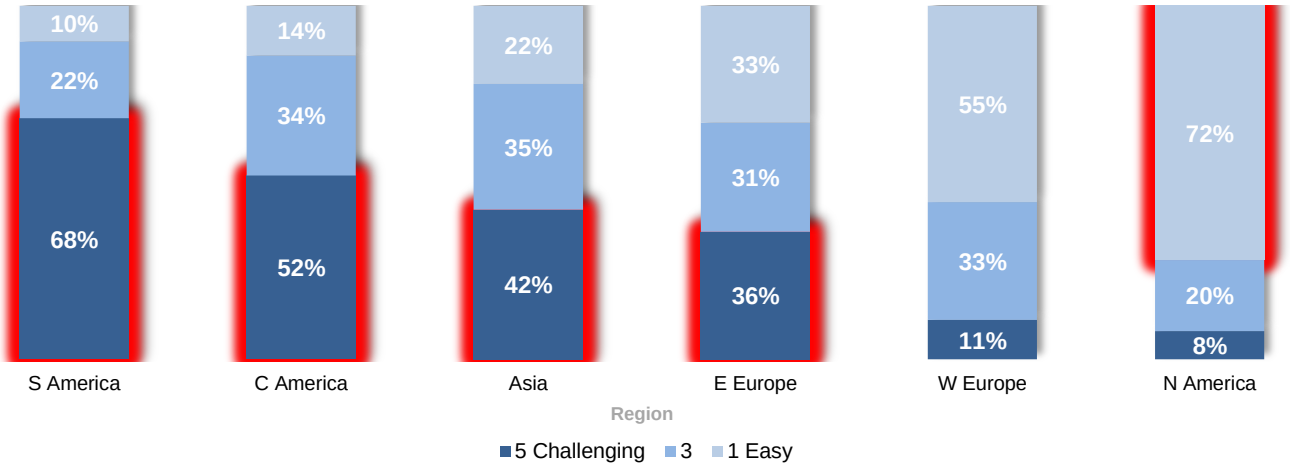
32% of survey respondents said they found logistics most challenging from the drug substance to drug product supply stage, followed by 31% for finished goods to local depot logistics stage. Half of participants stated that the least challenging drug supply stage was finished good logistics to central depot (Fig. 9).

Fig. 9: Degree of logistics challenge by drug supply stage



Over two thirds of participants cited South America as the most challenging region for logistics between depots to clinical sites, followed by Central America 52%, Asia 42% and Eastern Europe 36%. North America and Western Europe presented the least challenging regions for clinical trial logistics (Fig. 10).

Fig. 10: Logistics challenge between depot to clinical sites by region



Advisory Panel Insight

- *It is interesting given how prominent global clinical trials are and for how long companies have engaged with other countries outside of the US and Western Europe, that distribution still remains so challenging for all of us.* *(Catherine Hall, Director of Operational Excellence, Sunovion Pharma)*
- *We absolutely see the increase in variation of countries utilized. Sponsor companies do well when they engage supply chain partners to identify the optimal path and methodology at the planning stages. This can save considerable headache when the study gets underway.*

  (Brian Keesee, General Manager, US Clinical Services, PCI)

3.2c Use of an Import Broker

The increasing globalization of clinical studies, particularly by SME into pharmerging markets like Asia, Latin America and Eastern Europe present a number of diverse challenges, such as changing cultures, science, ethics, legislation and logistics infrastructure.

The survey indicates widespread use of clinical trial supply partners, with 86% of respondents using an import broker to overcome regional challenges such as compliance with import/export regulations for shipments of clinical trial supplies (Fig. 11).

Fig. 11: Type of import broker used

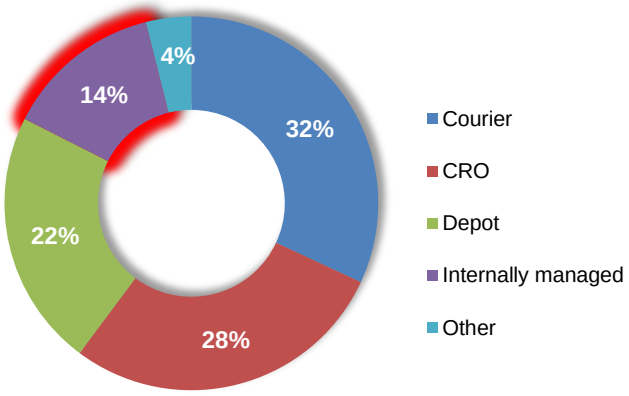
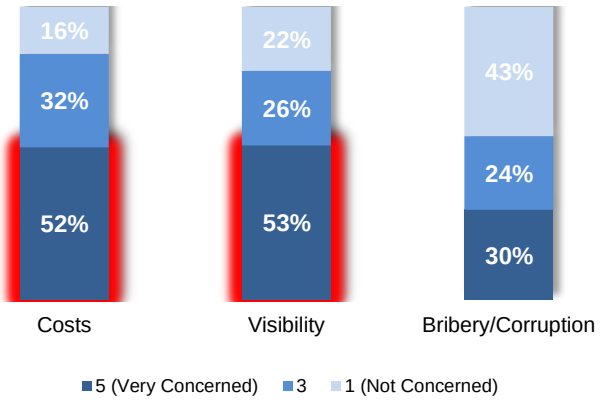


Fig. 12: Areas of concern associated with import brokers



Around half of respondents stated their main concerns with using a broker (Fig. 12) were cost control and levels of visibility offered by specialist service providers.

Access to trial data, especially when outsourcing supply activities is a key theme in this survey. Larger organizations have wider access to a single global technology platform, allowing easier data collection compared to trials run by smaller organizations that operate with multiple disparate systems, contributing to loss of data and lack of supply chain visibility.

Advisory Panel Insight

- *One of the biggest concerns with outsourcing in general is visibility and cost control. Who is acting on the company's behalf can vary from country to country and trial to trial. We all should continually be concerned with corruption, as a lack of diligence by any one of us can have grave consequences for all of us.*
  (Catherine Hall, Director of Operational Excellence, Sunovion Pharma)
- *These concerns are mitigated when using a trusted well vetted third party logistics provider, but always a risk. (Bob Albanese, Senior Vice President, Clinical Supplies Management)*
- *The trend is steadily increasing for use of emerging market geographies to lower cost and reach treatment naive patients. With this comes cultural differences, ever-evolving import/export needs, and other challenges. Brokers, combined with practical experience, can be useful to avoid roadblocks and delays in-country. (Brian Keesee, General Manager, US Clinical Services, PCI))*

3.2d Direct-to-Patient Distribution

Around a quarter of those surveyed use the Direct-to-Patient (DTP) distribution model for their clinical trial supplies (Fig. 13). From those not using DTP, one third of respondents said their company was 'likely' to consider it within the next 12-18 months (Fig. 14). The longer term implication of this trend would see around 50% of the companies surveyed, using or migrating to the DTP model.

Fig. 13: Use of DTP shipments from a depot/clinical site to patients home

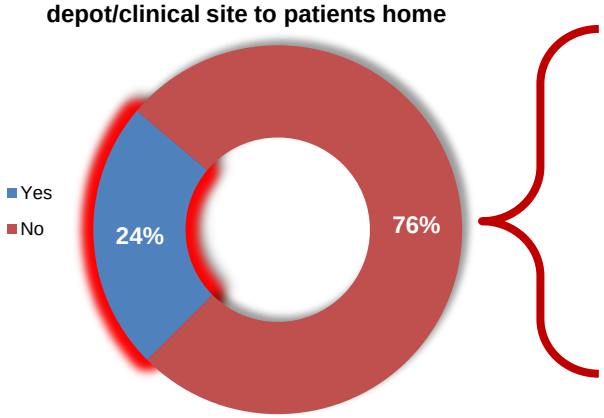
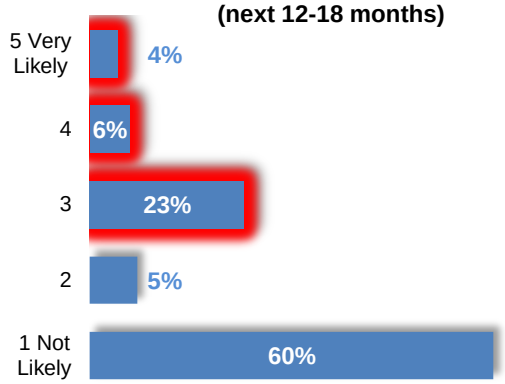


Fig. 14: % Likelihood of using DTP in future (next 12-18 months)



The survey revealed the main reasons stated for adopting DTP distribution (Fig. 15) were improved levels of patient retention by maintaining closer contact and offering more convenience 38%, followed by patients spread over wide geographical areas 19% and improved direct communication with patients 17%.

Fig. 15: % Reasons for shipping DTP

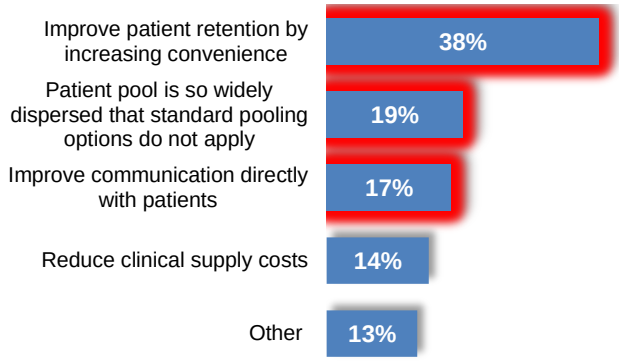
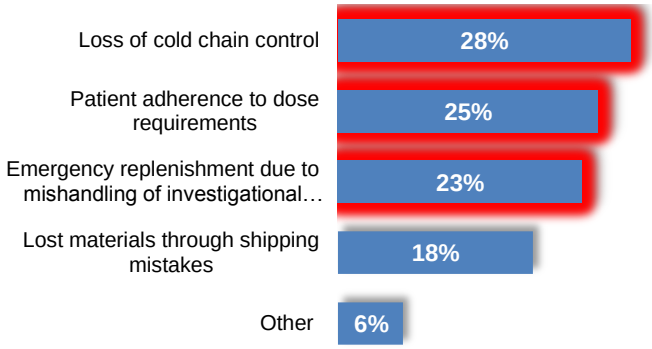


Fig. 16: % Risks of shipping DTP



Respondents stated that the main risks associated with DTP distribution (Fig. 16) were the lack of control in the 'last mile' concerning temperature sensitive materials 28%, followed by patient compliance to trial protocols 25% and ability to expedite re-supply to individuals at short notice as a result of product loss/mishandling 23%.

Advisory Panel Insight

- *I am not surprised to see a low percentage of respondents involved in DTP, but I am surprised that more than half of those not doing it now feel they are unlikely to do so in the future. A focus on patient centricity in the industry is prevalent among the customers of a clinical supply chain. The benefits of Direct-to-Patient Distribution have been proven and those that ignore it may be at a disadvantage soon.*

  (Catherine Hall, Director of Operational Excellence, Sunovion Pharma)

- *CSM only did DTP shipping originally for dispersed patient populations, but we are now seeing more activity around patient centric services. We have not seen any change in loss of cold chain, actually this has been improved as patients no longer have custody of IMP from site to home on DTP studies.*

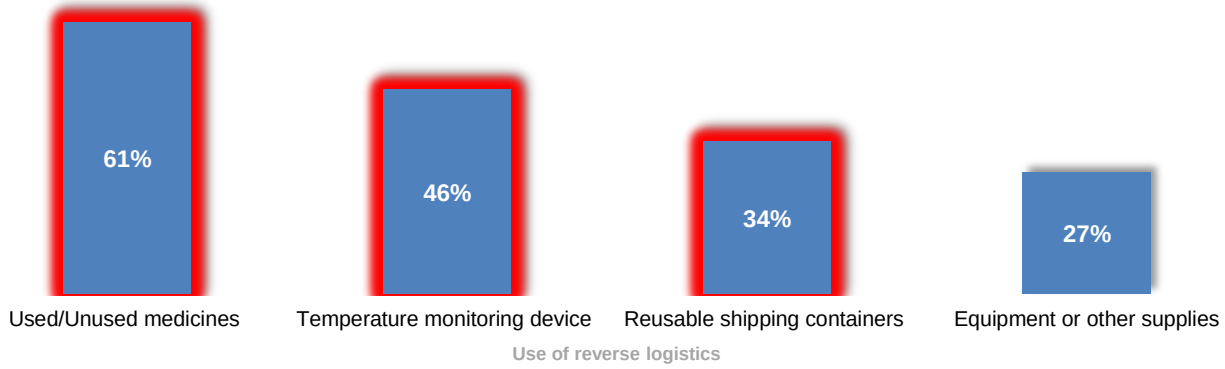
  (Bob Albanese, Senior Vice President, Clinical Supplies Management)

- *In our experience, Direct-to-Patient can be very effective. Advancing technologies can help provide the assurance about "The last mile" for Cold Chain concerns, as well as that of patient compliance and adherence to medication. Smart phone technology, in particular, has shortened the distance gap considerably. (Brian Keesee, General Manager, US Clinical Services, PCI))*

3.2e Reverse Logistics

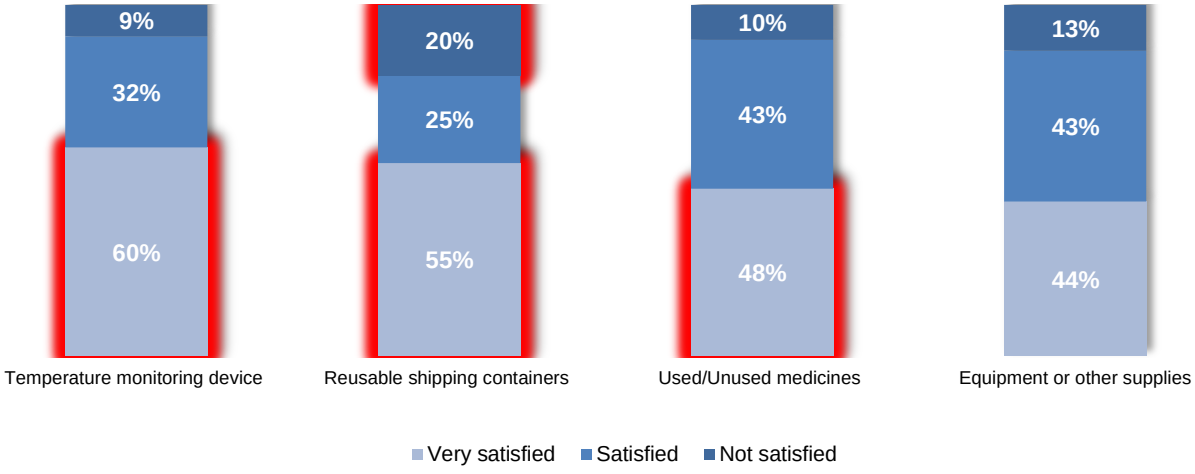
The respondents using reverse logistics (shipments from clinical sites to a depot or facility) showed that almost two thirds used it to recover used/unused medicines, followed by recovery of temperature monitoring devices 46% and for recovery of reusable shipping containers 34% (Fig. 17).

Fig. 17: Use of reverse logistics (shipments from clinical sites to depot/facility)



The greatest levels of satisfaction with reverse logistics (Fig. 18) were connected to recovery of temperature monitoring devices 60%, followed by reusable shipping containers 55% and recovery of medicines 48%. The highest level of dissatisfaction with reverse logistics was connected to recovery of reusable shipping containers 20%.

Fig. 18: Satisfaction with reverse logistics shipments



Advisory Panel Insight

- *Reverse logistics is a growing focus by regulators and clinical sites. Not only are sites concerned with the carbon footprint, but their ability to support destruction of supplies on site is less and less common, forcing sponsor companies to ensure reverse logistics are available and offers complete traceability to the regulators.* *(Catherine Hall, Director of Operational Excellence, Sunovion Pharma)*
- *In certain instances, reverse logistics can be an absolute necessity. Having a robust logistical plan with assured accountability is vital to avoid the headaches common to this exercise.*

  (Brian Keesee, General Manager, US Clinical Services, PCI)

3.3 Technology

3.3a Supply Chain Technology

Investments in data technologies to improve operational insights and efficiencies (Fig. 19) was highest by adoption of IRTs 25%, followed by Microsoft Office tools 24% and inventory systems/temperature monitoring database both at 13%.

Fig. 19: Supply chain technologies used

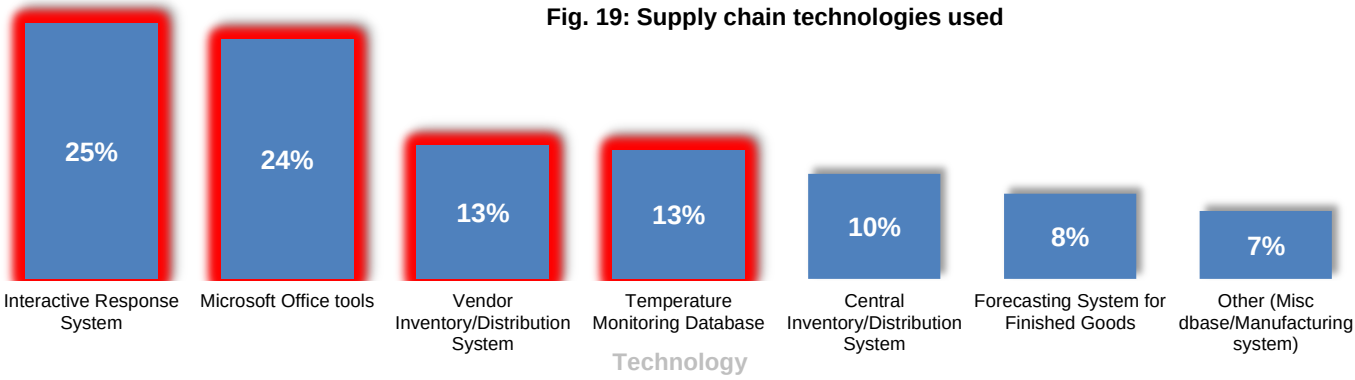
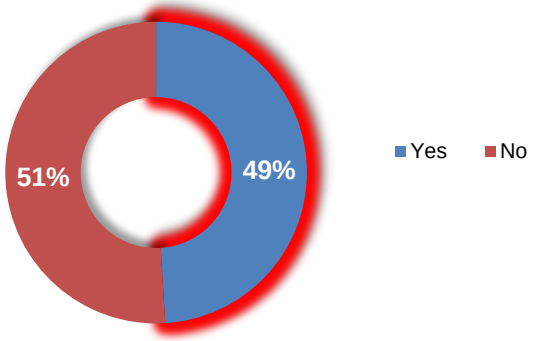
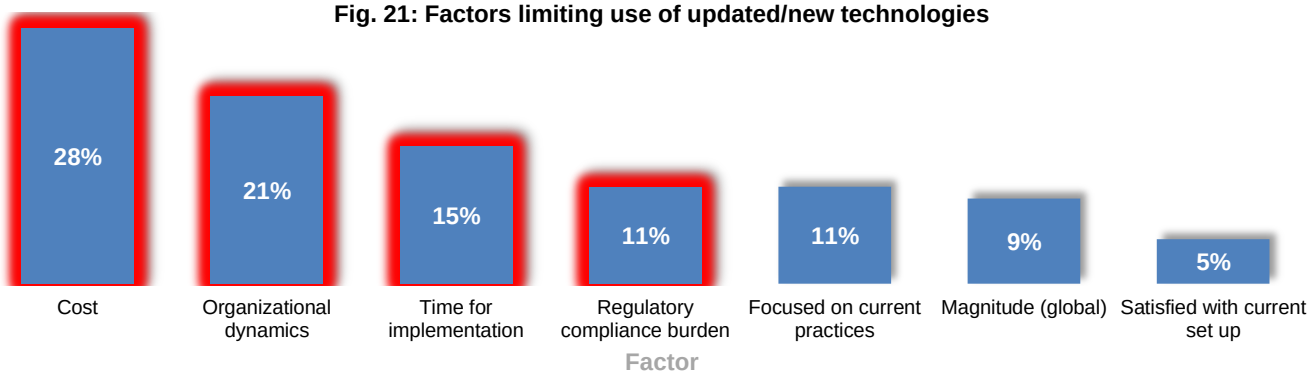


Fig. 20: Adoption of different technologies/info systems in next 12-24 months



Half of those surveyed said they would be adopting new technology with the next 2 years (Fig. 20), with the main barriers to adoption being cost 28%, team dynamics 21%, resourcing for global implementation 15% and responding to regulatory requirements 11% (Fig. 21).

Fig. 21: Factors limiting use of updated/new technologies



Advisory Panel Insight

- *It is interesting to see that so few respondents are happy with their current systems that less than half intend to implement new technologies in the next 2 years. Failure of our industry to invest in better technologies is a lost opportunity to innovate within the clinical supply chain space.*

  (Catherine Hall, Director of Operational Excellence, Sunovion Pharma)

- *We are seeing some noteworthy advances in technology, particularly in IRT, where a modular approach can significantly reduce leadtime for implementation and allow for study customization. We think this can be really impactful for integrating supply chains and site responsiveness.*

  (Brian Keesee, General Manager, US Clinical Services, PCI)

3.3b Mobile Technology

Over half of survey participants stated less than 10% use mobile technology in connection with their business activities (Fig. 22). More than two thirds stated that they plan wider adoption of mobile technology within the next 2 years (Fig. 23).

Fig. 22: Level of mobile technology use at work (excludes email & voice calls) % of respondents

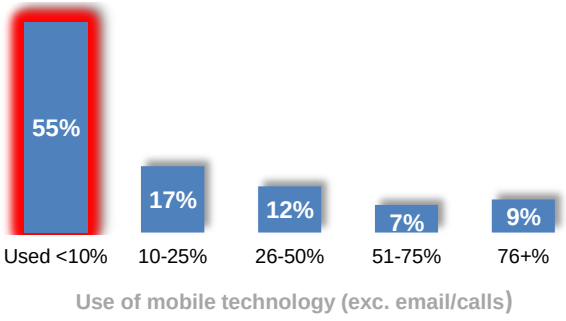
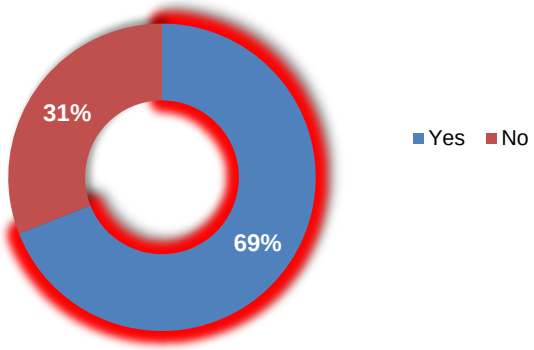
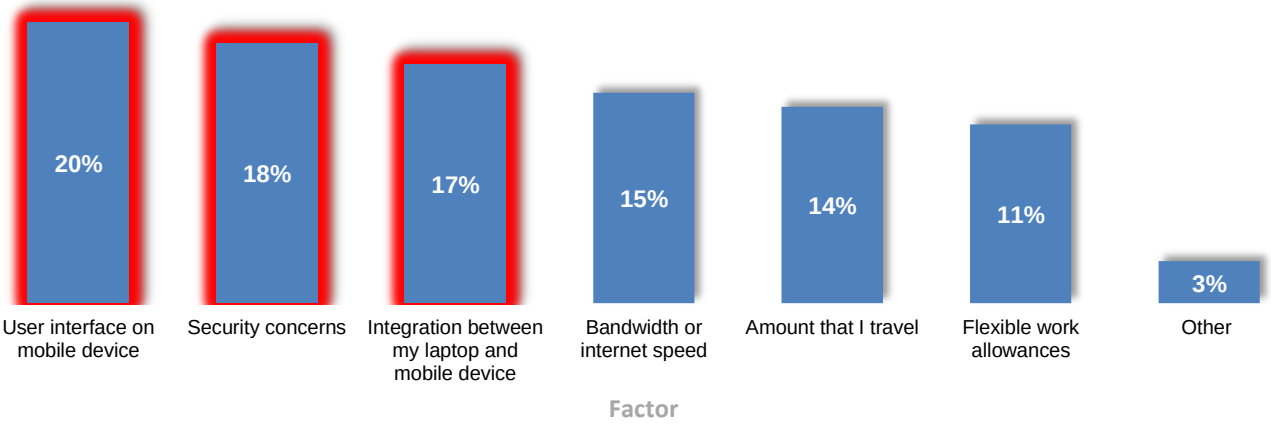


Fig. 23: Are there plans to expand use of mobile technology in next 1-2 years?



The survey asked what factors would impact wider adoption of new technology, 20% indicated a need for an easy to use interface on mobile devices, followed by 18% who were concerned about data security and 17% citing the ability to integrate data between different devices (Fig. 24).

Fig. 24: Factors impacting adoption of mobile technology at work



Advisory Panel Insight

- *Interesting contrast to a lack of focus on building better technologies, respondents feel a focus on going mobile is a future direction. Certainly the world is moving mobile, but core technologies need to exist first prior to having a mobile version.*

  (Catherine Hall, Director of Operational Excellence, Sunovion Pharma)

- *With the trend towards Patient Centricity we do see increased mobile engagement with patients/sites, but interestingly the industry has not broadly adopted mobile usage for supply chain visibility, particularly as the studies advance towards use of more distant countries.*

  (Brian Keesee, General Manager, US Clinical Services, PCI)

3.4 Supply Chain Challenges

Analysis of supply paths for non-investigational comparator products revealed that for three quarters of the distribution activity, 43% of the respondents source centrally and then distribute it to the clinical sites, 38% use third party sourcing, followed by 18% who source locally and then distribute it to clinical sites and 15% source directly at the clinical site (Figs. 25 to 28).

Fig. 25: % Survey responders using central source & distribution to sites

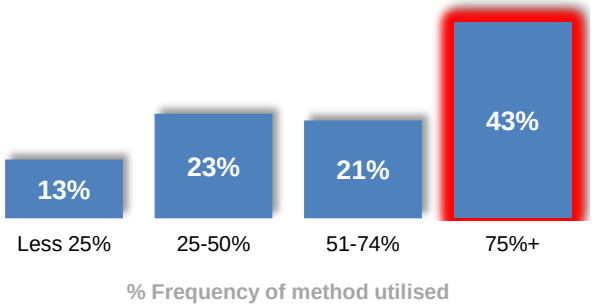


Fig. 26: % Survey responders using local source & distribution to sites

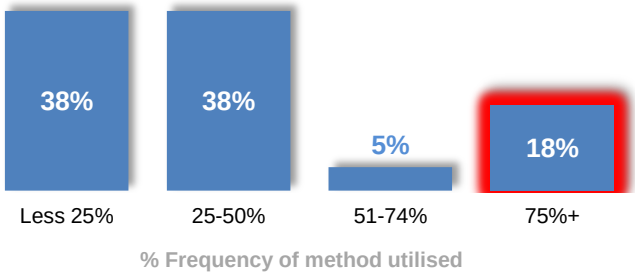


Fig. 27: % Survey responders using third party source

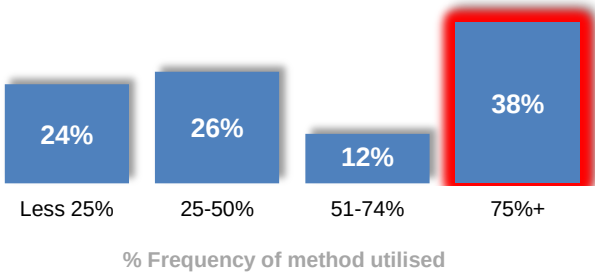
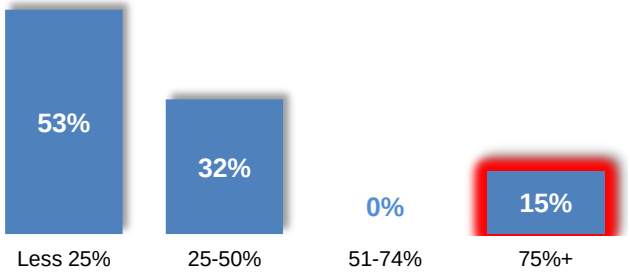


Fig. 28: % Survey responders using site source



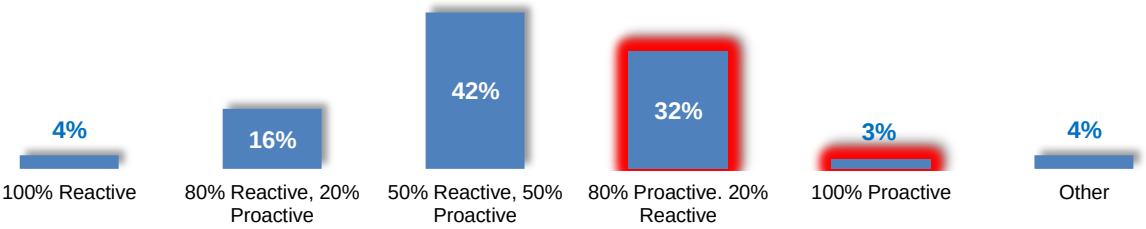
Advisory Panel Insight

- *Comparator sourcing and distribution remains variable in our industry, this invites more attention to determine true best practices.* *(Catherine Hall, Director of Operational Excellence, Sunovion Pharma)*

3.4a How Proactive Is Your Supply Chain?

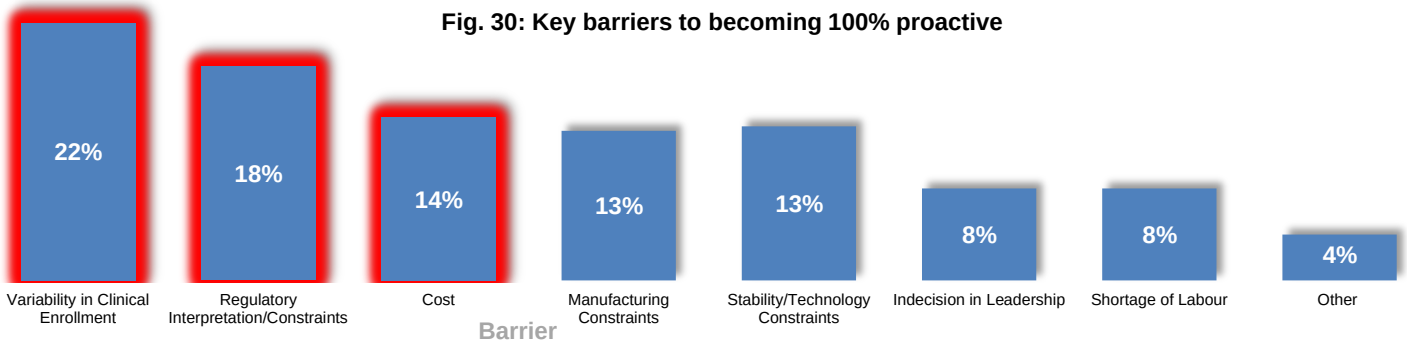
35% of the respondents felt that their supply chain was more proactive than reactive (Fig. 29). This implies that there is scope for further improvements towards creating a more proactive supply chain.

Fig. 29: How would you describe your supply chain?



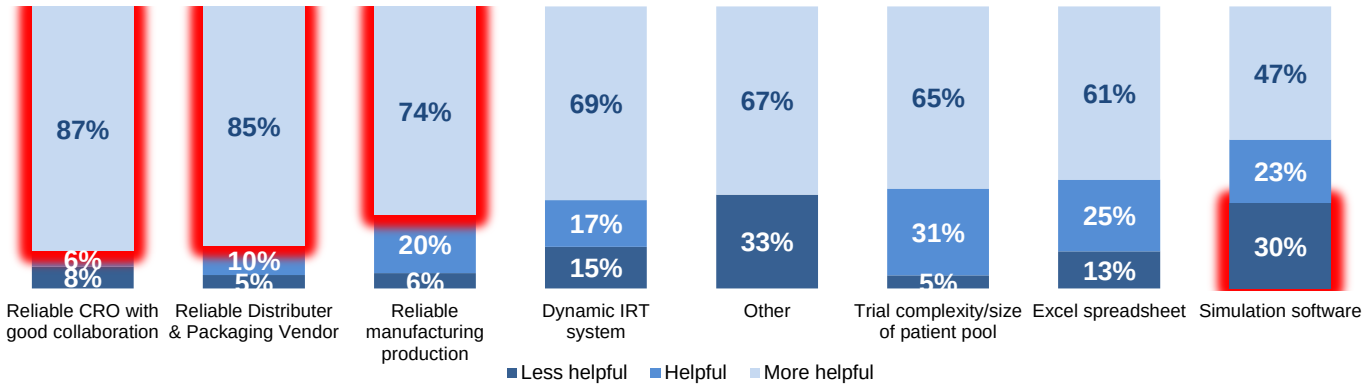
The main barriers cited for the supply chain to become more proactive included varying supply demands in clinical enrolment 22%, followed by regulatory compliance 18% and cost implications 14% (Fig. 30).

Fig. 30: Key barriers to becoming 100% proactive



Close and reliable partnerships between clinical and operational teams were cited as the most important factor in successful supply forecasting: relationships with CRO 87%, distributor/packaging supplier 85% followed by the manufacturer 74%. Supply forecasting was least assisted by use of simulation software 30%.

Fig. 31: Degree of impact tools have on successful forecasting of clinical trial supplies



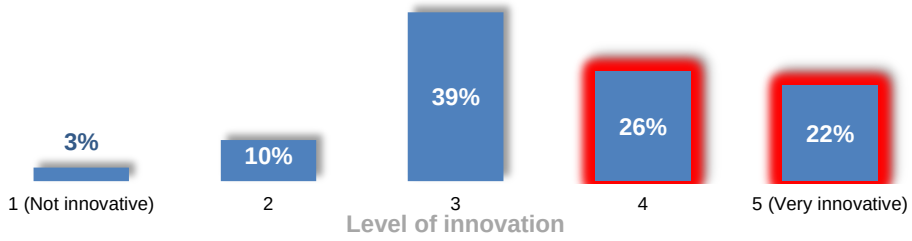
Advisory Panel Insight

- *Probably the least progress we have made in our industry is w.r.t. moving towards a proactive clinical supply chain. That we still feel victim to unpredictable enrolment where only strength in collaboration with CROs and CMOs is seen as the answer, indicates how much more work we need to do together to help improve our processes and tools.* *(Catherine Hall, Director of Operational Excellence, Sunovion Pharma)*

3.5 Innovation

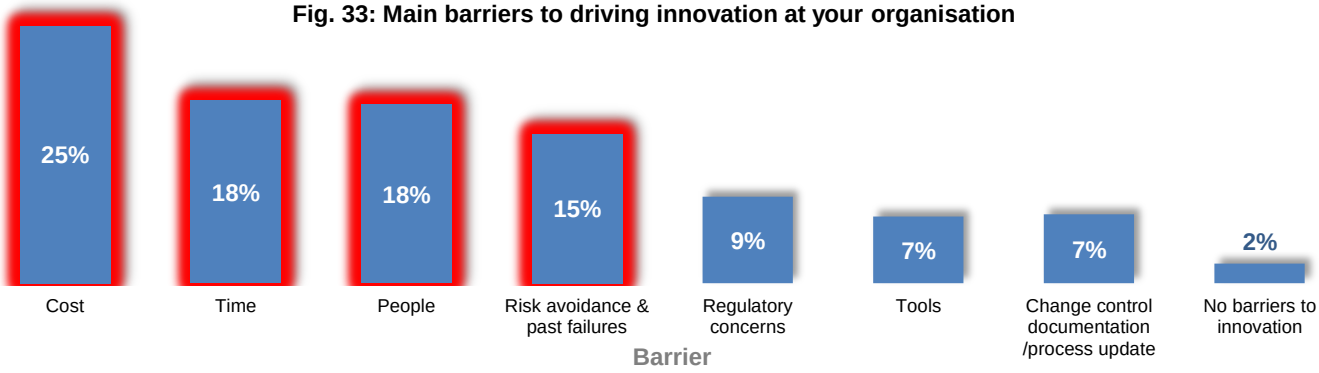
Around half of those surveyed thought their organizations were quite innovative, while the remaining half indicated that there was scope for further improvement (Fig. 32).

Fig. 32: How innovative is your organization?



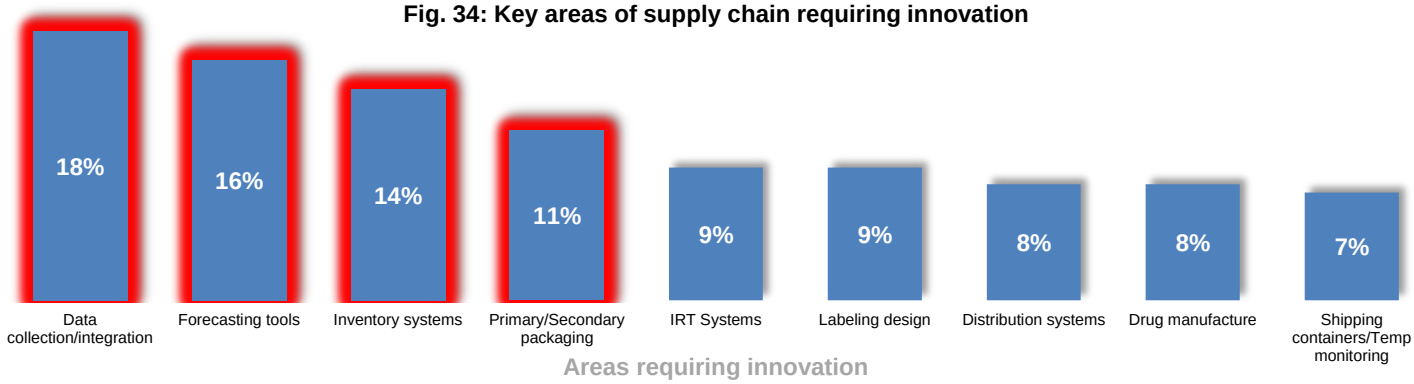
When looking at the barriers to drive further innovation, one quarter of respondents cited cost as the main factor, followed by time 18%, people 18% and internal culture towards taking risks 15%. Only 2% of those surveyed stated there were no barriers to adopting supply chain innovation at their organization (Fig. 33).

Fig. 33: Main barriers to driving innovation at your organisation



The main aspects of supply chain that could leverage new technology were data integration 18%, followed by forecasting tools 16%, inventory systems 14% and packaging 11% (Fig. 34).

Fig. 34: Key areas of supply chain requiring innovation



Advisory Panel Insight

- *There are huge barriers to driving innovation. That a majority feel their organizations are innovative yet still largely reactive in nature is a striking dichotomy. Not surprising that better data and forecasting tools remain top wants in supply chain.* *(Catherine Hall, Director of Operational Excellence, Sunovion Pharma)*
- *CSM also believes that data integration is key to successful supply chain control. Being in the middle of the supply chain means that we need integration both upstream and downstream, allowing proactive change to known conditions.* *(Bob Albanese, Senior Vice President, Clinical Supplies Management)*

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