TMF Futures 2021: Good data in the age of digital transformation

arkivum

Bringing archived data to life

Contents

Foreword: Chris Sigley, CEO Arkivum

This second annual TMF Futures report bears witness to a period of rapid transformation. Emerging from the pandemic, teams that run and assess clinical trials can take stock of the way they have risen to the challenges faced since early 2020.

Over that time, digital technology – both established and innovative – has played a crucial role in overcoming physical interruptions and bottlenecks. Applied resourcefully, it has both ensured the continuity of clinical trials and laid foundations for future ways of working.

Through all this, good practice has remained a touchstone for every organisation in life sciences. Just as there are trusted protocols and processes for gathering clinical-trial data – a highly valuable asset – so there are for managing it, both during and after the trial. At the height of the pandemic, COVID-19 kept patients in their homes.

Regulators and clinical trial stakeholders rapidly accelerated patient access to telemedicine; they also decentralised clinical trials. Initiatives of this kind rely on a rigorous approach to the collection, exchange and storage of clinical data. Good practice of this kind will help to ensure that data has a long and potentially highly productive life, whether it is serving scientific, regulatory or commercial purposes. Providing it is stewarded in a way that ensures its security, integrity, accessibility and usability, its lifecycle can extend over several decades – or even indefinitely.

At Arkivum we are committed to upholding good practice, and to furthering transformation, with our dedicated digital archiving solution for the eTMF and other forms of clinical-trial data. Certified to international standards (ISO 9001 and ISO 27001), it aligns to the TMF Reference Model, and, through its frequently validated CSV releases, complies with the requirements of the FDA, EMA, MHRA and other national regulators. As a fully managed, end-to-end service, it streamlines complex workflows and regulatory processes.

In a transformed world, further empowered by digital technology, the life sciences industry is in a position to come back stronger than ever before. Whatever new challenges it faces over the coming years, Arkivum is ready to support it in making the most of its assets, expertise and opportunities.

Introduction

Arkivum's second annual TMF Futures report updates, supplements and amplifies the findings of the first report, published in September 2020. It comes after a period of more than a year which has brought unprecedented challenges for clinical trials and the dramatic acceleration of digital transformation in virtually every major industry.

Against this background, life sciences organisations running clinical trials continue to strive for greater productivity in the trial process and to find new and better ways of working. Currently, the research and development cost of bringing a new medicine to market is estimated at USD 1.3 biillion.[1]

As in 2020, the fundamental premises of the report are that:

i) The trial master file (TMF) is a central discipline of drug development, playing a crucial and durable role in the regulatory process.

ii) The disciplines of data management and data governance, again functioning within a strict regulatory framework, are essential to the success of life sciences organisations in deriving maximum knowledge from their information and maximum value from their intellectual property.

Since the publication of the 2020 TMF Futures report, times have remained challenging for clinical trials. The global pandemic caused many trials to be stalled or cancelled. Patients, often suffering from chronic and life-threatening conditions, were unable to access trial treatments[2], while sponsors and CROs struggled to identify, recruit and treat participants[3].

In response to the pandemic, and to get trials and business operations back on track, life sciences and biopharma – at great speed and cost[4] – pivoted and embraced new digital technologies. While looking to protect itself against further COVID-induced economic shocks, the life sciences sector is, as ever, concerned with managing R&D costs and overcoming hurdles to market access.[5]

The moment for digital transformation has clearly arrived for the sector. Every major clinical trial sponsor is now running at least one decentralised clinical trial, and innovation offers the prospect of reduced costs and tighter schedules for clinical trials, and also of reduced risk of failure, thanks to the potential of such technologies as artificial intelligence (AI).[6]

This 2021 report is drawn from the second annual TMF Futures survey. Polling the views of 300 life sciences professionals in April 2021 (some 12 months into the global pandemic), it tracks the progress of life sciences and biopharma companies over the past year as they implement digital transformation strategies and unlock the potential of their clinical trial data. The report confirms that many life sciences organisations are accelerating digital transformation to increase efficiencies, enhance collaboration, and modernise and improve the clinical trial process.

Digital transformation will serve primarily to:

- Improve the way the life sciences sector identifies and communicates with health care professionals and patient populations (50% of survey respondents cited this).

- Improve archiving and integration of the eTMF and other data on a large scale (38%).

- Further the adoption of decentralised trials (34%).

When conducting clinical trials, the majority (90%) of life sciences organisations continue to face challenges. With the aim of reducing the cost and duration of clinical trials – and of increasing their chances of success – eight in ten (80%) life sciences organisations plan to invest significantly in technology (e.g. artificial intelligence, machine learning and cloud computing) in order to interrogate clinical data.

That being said, the survey reaffirms another key finding of last year's TMF Futures report: the fragility of certain critical systems in the clinical trial process, notably a lack of interoperability between eClinical systems. (This issue is central to the development, launched in 2018, of the Exchange Mechanism Standard as part of the TMF Reference Model: "…the problem of exchanging TMFs between different vendor systems remains, due to the lack of a common exchange standard.") Over half of life sciences organisations confirm that sub-optimal processes for data transfer from site investigators to the CRO and sponsor, and for storage, are potentially compromising the integrity and inspection-readiness of the eTMF.

Clearly, this can result in breaches of regulatory compliance, undermining progress that has been made and causing delays to marketing authorisation applications (MAA). This comes at a time when the FDA plans to adopt electronic tools and when it is evaluating the disruptive impact of COVID on clinical trials – for instance on the quality of clinical data and the integrity of the trial.[7]

In October 2020, the management consultancy McKinsey reported that across industries, COVID-19 has accelerated the adoption of digital strategies by as much as seven years.[8] Life sciences companies clearly stand to benefit from further adoption of data and predictive analytics, cognitive automation, AI, cloud computing, and other new technologies to accelerate scientific discovery and increase productivity and reduce inefficiencies.

In the meantime, many life sciences and biopharma companies continue to struggle to access, interrogate and protect existing clinical trial data in their eTMF archive. These shortcomings both engender regulatory risk and compromise the commercial value of archived data.

The importance of data and the eTMF

The TMF archive has to fulfil both regulatory and commercial objectives, while being responsive to novel trial designs and supporting post-market safety, regulatory decisions, and label expansions.

The life sciences sector has faced many obstacles over the past year, but it has also been a time of progress and transformation: randomised evaluations of COVID-19 vaccines and therapies were organised in a matter of days; globally, it became clear that reaping the full benefits of clinical trials – in the form of approved vaccines and therapies – is dependent on collecting trial data in the right way.

- An example of success in handling data

Analysis of data from patients prompted physicians to rapidly establish a multi-national randomised controlled trial (RCT) which found that the generic steroid dexamethasone was highly effective as a treatment for severe COVID-19. As a consequence, a million lives were saved.[9]

- An example of failure in handling data

In the UK, records of almost 16,000 positive COVID-19 cases disappeared during transfer between testing labs and England's contact-tracing system. They had been stored in an outdated Excel file format with insufficient capacity.[10] The consequences were fatal. The economists Thiemo Fetzer and Thomas Graeber estimated that this data mishap led to 125,000 further cases and 1,500 deaths.

Inspection-readiness is the primary aim when archiving the **Trial Master File (TMF**) – the collection of essential documents and data relating to a clinical trial, which over the past decade has moved to a digital format (**eTMF**). In other words, the priority is to ensure that data is in a fit state for formal review by inspectors from official bodies. The key aims of the inspection are to verify:

i. Whether the sponsor and investigators have conducted the trial in line with regulatory requirements and the principle standards of Good Clinical Practice (GCP).

ii. That the data obtained has been validated and stored correctly. If it has not, the TMF can fail the inspection, with the consequence that drug approval is denied.

In a world of digital transformation and technological acceleration, the potential of the eTMF beyond its core regulatory mission is becoming strikingly evident. Living data in the eTMF archive now plays an increasingly important role in extending the applications of certain treatments. Over the last year a total of four in ten life sciences organisations have needed to access the TMF archive in order to locate data to support new submissions (34%), new indications (31%) and repurposing (7%). This compares to the 26% of life sciences organisations that accessed the archive in the context of a regulatory inspection.

Meanwhile, advances in gene and cell therapies and 'omics' technology and data have led to a rise in personalised medicines and biomarker-based strategies. Increasingly, real world evidence studies (where evidence is collected on an ongoing basis rather than through pre-approval RCTs) are serving the cause of post-market safety, regulation, and label expansions for rare disease – a field in which patient populations are small and diverse. All this requires the archive to be responsive and far more than the 'locked box' of tradition.[11, 12]

When it comes to digital archiving, the survey suggests that there is still much room for progress in maintaining a secure archive which offers sufficient functionality both i) to ensure long-term inspection-readiness, and ii) to enhance potential for extending the lifecycle and commercial potential of approved medicines (for instance through new indications and formulations, or licensing and partnership opportunities).

In light of this, it becomes questionable whether current archiving practice across the sector consistently conforms with the ALCOA+ and FAIR principles of data management[13,14], or with the EMA's stipulation in its 2018 TMF guidance that, "the dynamic character of the audit trail should be preserved, when applicable."[15]

If the life sciences sector is to 'come back stronger' after COVID-19, it requires good data at every point.
All in all, however, few archives currently offer sufficient capability to meet the needs of the sector. Only a small number of life sciences organisations demonstrably run a digital archive which is built on FAIR data principles to ensure data is Findable, Accessible, Interoperable, and Re-usable.[16,17]

Complementing the FAIR principles is ALCOA+, originally established by the FDA with the aim of ensuring data integrity in such areas as pharmaceutical research:
This 2021 TMF Futures report examines:

ALCOA	+
ATTRIBUTABLE LEGIBLE CONTEMPORANEOUS ORIGINAL ACCURATE	COMPLETE CONSISTENT ENDURING AVAILABLE

i. The impact of COVID-19 on clinical trials and the strategies adopted by global life sciences companies in order to 'come back stronger';

ii. The progress made by global life sciences companies in the adoption of digital transformation strategies;

iii. The priorities, challenges and necessary advances for companies wishing to maintain their TMF archive in a constant state of inspection-readiness, while also aligning their digital archive and clinical data to their broader commercial goals and objectives.

Survey Methodology

The second annual Arkivum TMF Futures survey was conducted in April 2021 by Arkivum.

The objectives of the survey were to provide insight into:

i. The clinical trial data strategies adopted by global life sciences organisations, and

ii. The priorities, challenges and necessary advances for companies wishing to maintain their eTMF archive in a constant state of inspection-readiness, while also aligning their digital archive and clinical data to their broader commercial goals and objectives.

The survey comprised 20 questions falling into five sections:

i. The impact of COVID 19 on clinical trials; Kick-starting clinical trials; 'Coming back stronger;'

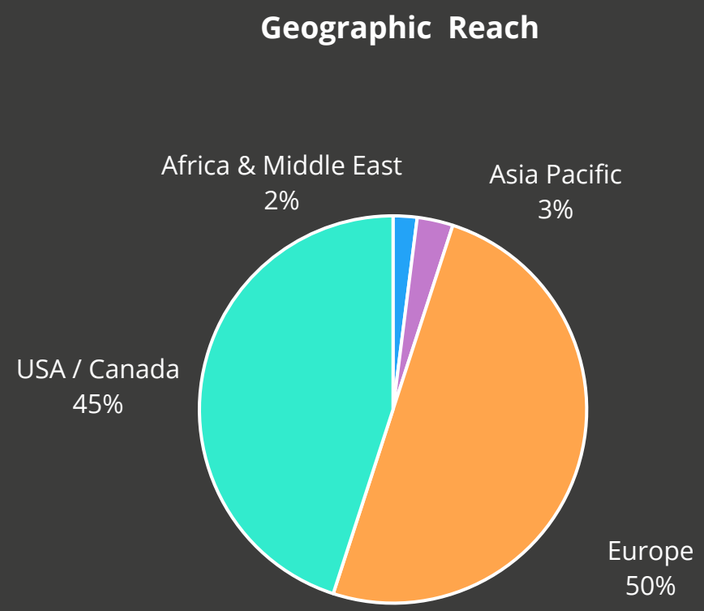
ii. COVID-19: The catalyst to accelerate the adoption of digital technology;

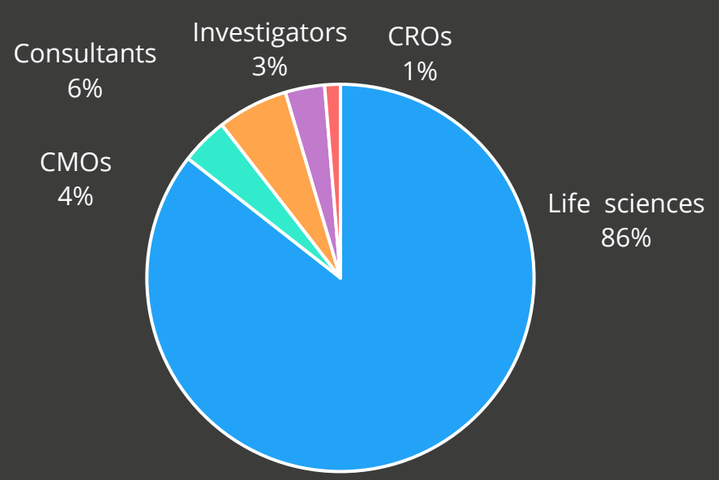
iii. eTMF: Barriers to managing data and documents in clinical trials;

iv. eTMF Digital Archive: Meeting regulatory objectives;

v. eTMF: Adopting technology to create a fit-for-purpose digital archive.

The 305 senior representatives surveyed have responsibility for/knowledge of clinical trials and hold senior and director-level positions in the following functions: General and senior management, Regulatory;, Quality Assurance, Medical Affairs, Clinical Operations.





Notes: 2021: 305 responses, comprising 261 life science companies, 12 CMOs, 18 consultants, 10 investigators, 4 CROs
Source: Responses to Arkivum and Survey Goo

Survey Objectives

The survey sought to probe life sciences professionals' views on:

CLINICAL TRIALS

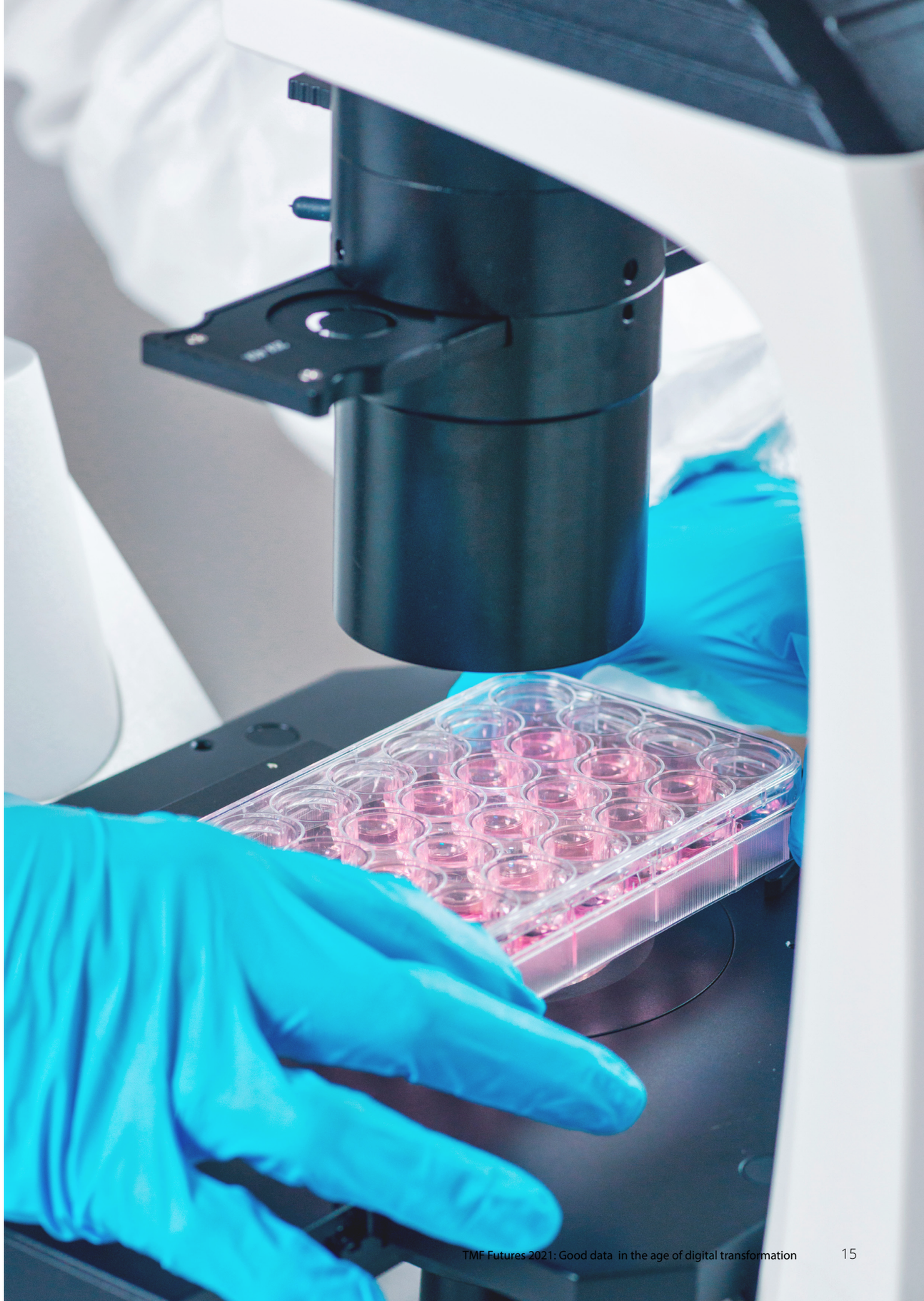
- The impact of COVID-19 on clinical trials.

DIGITAL TRANSFORMATION STRATEGIES

- The adoption of digital systems and strategies to collect, exchange, store and interrogate data and documents (Trial Master File: TMF/eTMF).

DIGITAL ARCHIVE

- Keeping clinical data from past trials alive in order to meet the demands of the long-term regulatory environment (which prescribes a continuous state of inspection-readiness for 25 years), while simultaneously serving the broader commercial objectives and goals of the organisation.



Summary of key findings

What has been the impact of COVID-19 on clinical trials and what strategies have been adopted by global life sciences companies as they aim to ‘come back stronger’?

- Half (56%) of life sciences organisations say that COVID-19 has had a negative impact on their ability to deliver on the objectives of their clinical trials, compared to three out of four (69%) in August 2020.
- In 2020, 41% of new clinical trials were delayed or put on hold indefinitely. Four in ten (41%) of these cancelled/delayed clinical trials will now be run in 2021.
- Life sciences organisations have pivoted to technology to get their trials and operations back on track, but nearly six in ten (57%) now say the cost of running a clinical trial has increased. 188 billion USD was spent on R&D in 2020.
- These rises have been partly offset by: cuts from other budgets (45%), reduced travel and cancelled congresses (15%), cuts to shareholder profits (17%).

What progress has been made by global life sciences companies in the adoption of digital transformation strategies?

- Eight in ten (75%) life sciences organisations plan to invest significantly in technology (e.g. artificial intelligence, machine learning and cloud computing).

- Seven in ten organisations (70%) are likely to make a large investment in technology to enable interrogation of clinical data on a large scale, with the aim of furthering scientific discovery and meeting regulatory requirements, while bringing down the cost and time it takes to conduct a clinical trial.

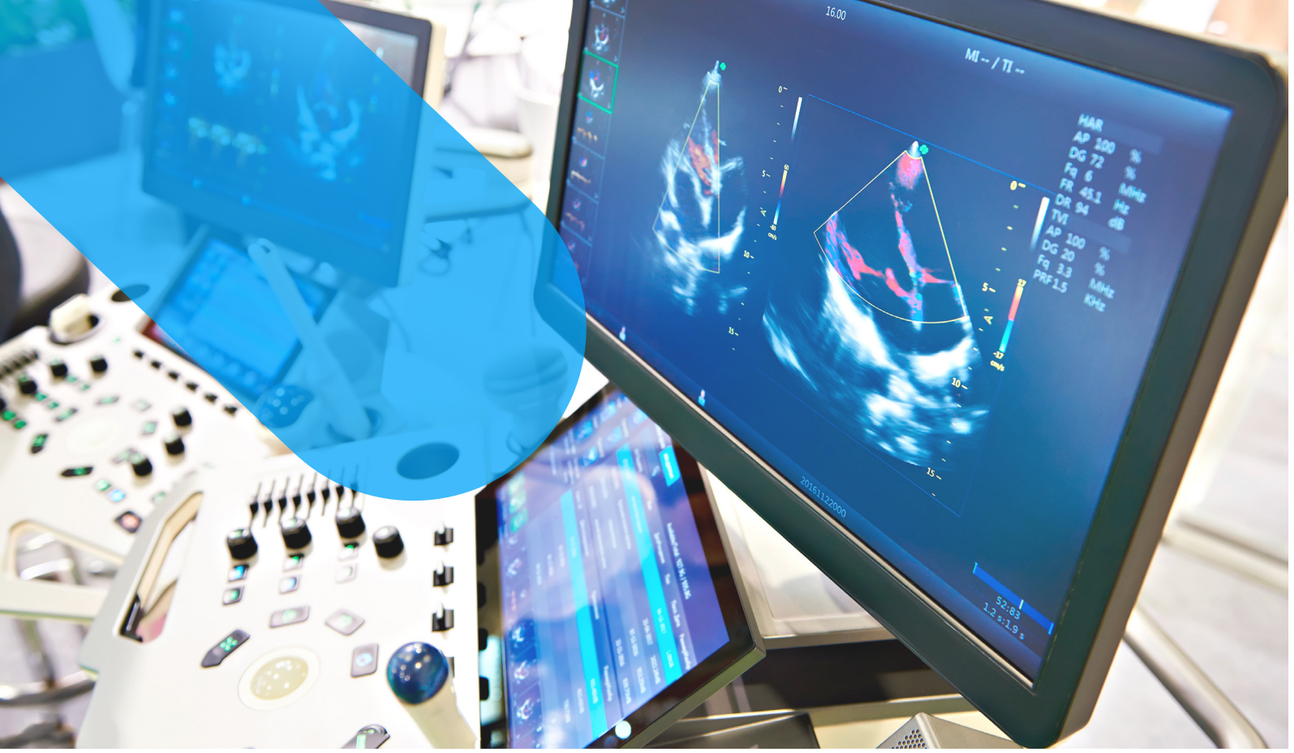
- As the life sciences sector embraces new strategies to improve the way clinical trials are conducted, the priorities for clinical trials are now to:

  - Continue the decentralisation of clinical trials – increase remote treatment and monitoring (47%);

  - Increase racial diversity (34%) and geographic reach (26%) in enrolment of clinical trial patients;

  - Adopt new technology such as AI, machine learning, and cloud computing to aid the conduct of trials and the management of data (34%).

  - Implement archiving technology to facilitate remote inspections (18%).



What are the priorities, challenges and necessary advances for companies wishing to maintain their TMF archive in a constant state of inspection-readiness, while also aligning their digital archive and clinical data to their broader commercial goals and objectives?

- The eTMF is growing in complexity and size. The average eTMF runs to 10,500 documents and 46% of eTMFs now comprise 50,000 documents or more.

- 16% of life sciences organisations now plan archiving of the eTMF at the pre-clinical stage (Phase 0), or at the start of the Phase I trial (17%). The majority (40%) start archiving at the start of the Phase II trial or later. But, in order to ensure that the original file is built to the right standards and stored in the right way, data needs to be continuously curated and managed in accordance with prevailing regulations.

- The EU directives state that the TMF archive must be maintained for 25 years. However, 66% of life sciences organisations say they cannot guarantee that their eTMF archive will keep their data secure, accessible and usable for 25 years (as stipulated by the EMA), and few have an archive that is FAIR (i.e. data is Findable, Accessible, Interoperable, and Re-usable).

- Nearly all (90%) life sciences organisations have a digital archive, but only half (53%) would describe their eTMF archive as compliant and fit for purpose, ensuring inspection-readiness for 25 years (as stipulated by the EMA); the proportion drops to 37% among regulatory and compliance professionals.

- 80% of regulatory and compliance professionals (vs 30% of all respondents) describe their TMF archive as very or extremely inadequate.

- 55% of life sciences organisations say sub-optimal processes for data transfer from site investigators to the CRO and sponsor, and for storage, are compromising the integrity of the eTMF, resulting in breaches of regulatory compliance.

- Just half (48%) of life sciences organisations say that, if they were inspected tomorrow by a regulator, they would be extremely or very confident their eTMF would pass an inspection and not be subject to a critical finding.

- A quarter (26%) of life sciences organisations have accessed the archive for purposes of a regulatory inspection over the past 12 months; but if all reasons for accessing the archive are taken into account, they are more likely to do so for purposes other than compliance. Among these are: new formulations (34%); indications and repurposing (32%); market access (21%), and patient safety (15%). There is an increasing need to access archived data for commercial purposes, such as legal challenges (21%), licensing (19%), and due diligence for multi-million/billion mergers and acquisitions (12%).

The archive now also stores data other than the eTMF, including patient data (62%), lab data (40%) and genomic data (20%). Half (53%) of respondents say that storing patient data presents the greatest regulatory risk to their organisation.

Key findings in full

i. The impact of COVID-19 on clinical trials

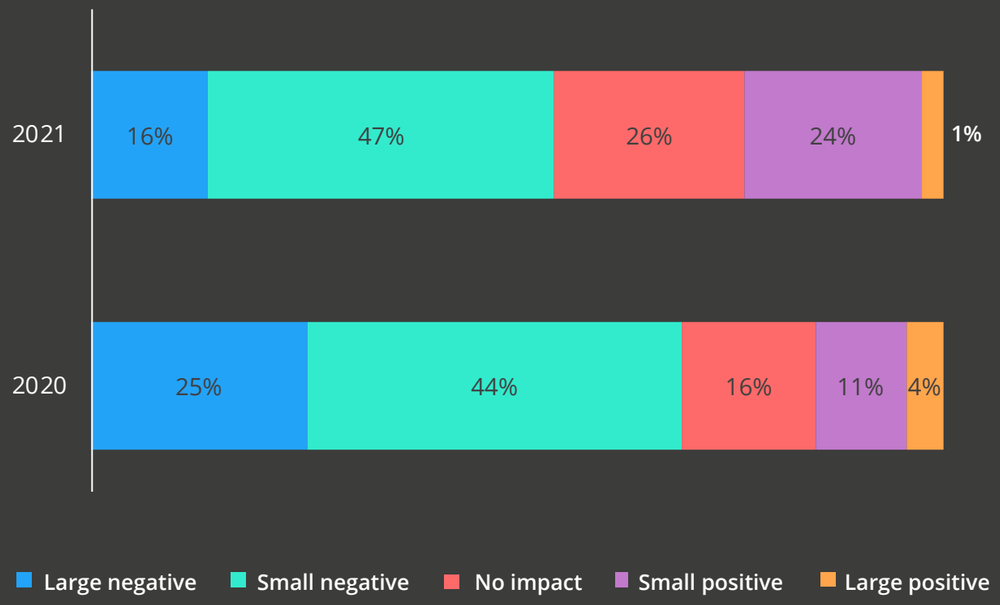
As a consequence of COVID-19, the life sciences industry has experienced major disruption to clinical trials. For instance, during the first wave of the pandemic, 84% of rare disease patients in Europe – many of whom are enrolled in clinical trials – experienced a disruption of care, including reduced access to diagnostic tests and therapies such as chemotherapies and infusions. [1]

In July 2020, the life sciences industry said cancellations were likely to remain the greatest setback to clinical trials. But in 2021, after the industry pivoted at great speed (and expense) to get its trials back on track, just half (56%) of life sciences organisations say that COVID-19 has had a negative impact on their ability to deliver on the objectives of their clinical trials; this compares to three out of four (69%) in August 2020.

Half (55%) of life sciences organisations say COVID-19 has had a negative impact on their ability to deliver on the objectives of their clinical trials, compared to three out of four (74%) in August 2020.

One in five (21%) say COVID has had a positive impact.

To what extent will COVID-19 affect your organisation's ability to deliver on its clinical trial objectives over the next six to 12 months?



Before COVID-19, 14,900 clinical trials were in progress globally (informa.com)[18], with each life sciences organisation planning to conduct 6.5 Phase I/II/III/IV studies this year. But as social distancing and lockdowns have been implemented across the world, four out of ten clinical trials in therapeutic areas other than COVID-19 have been delayed or put on hold indefinitely. 41% of these cancelled/delayed clinical trials will now run in 2021, with the industry running, on average, 4.68 Phase I/II/III/IV studies in the course of the year. 23% of these will be in next generation therapeutics, such as cell and gene therapies.

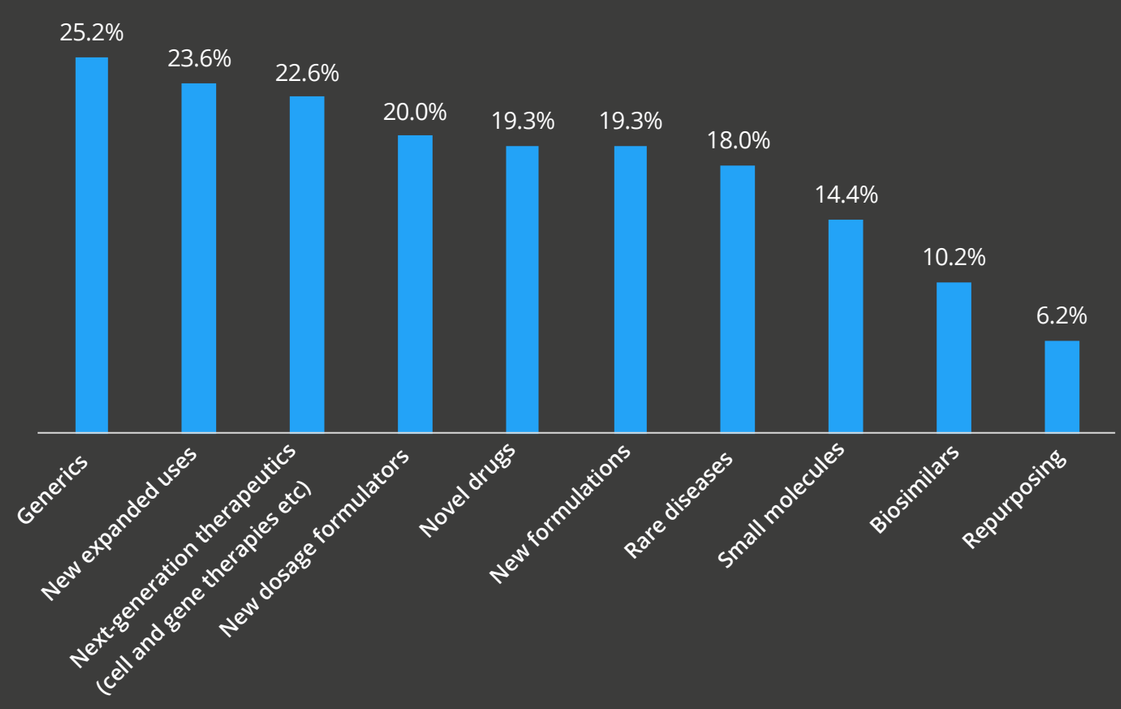
As a consequence of COVID-19, in 2020 41% of clinical trial start dates were delayed or put on hold indefinitely.

Four in ten (41%) of these cancelled clinical trials will now be run in 2021.

In 2020 life sciences organisations planned to conduct, on average, 6.5 Phase I/II/III/IV trials a year.

In 2021 the industry will run, on average, 4.68 Phase I/II/III/IV studies.

In which of the following areas are your clinical studies focused?

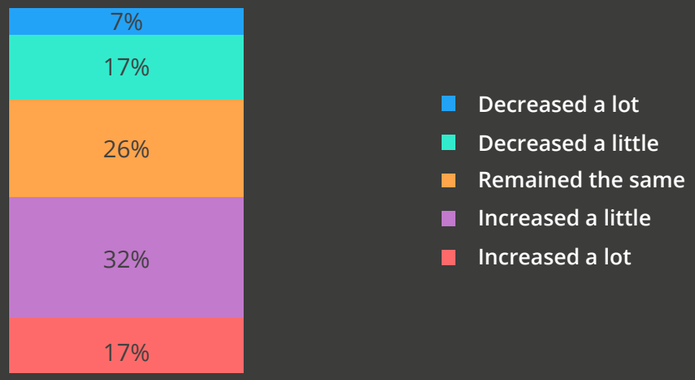


Despite valiant efforts to get trials back on track, life sciences organisations say that, since the start of the pandemic, there has been an increase in the time (49%) and cost (57%) for completing a clinical trial. (USD 188 billion was spent on R&D in 2020).

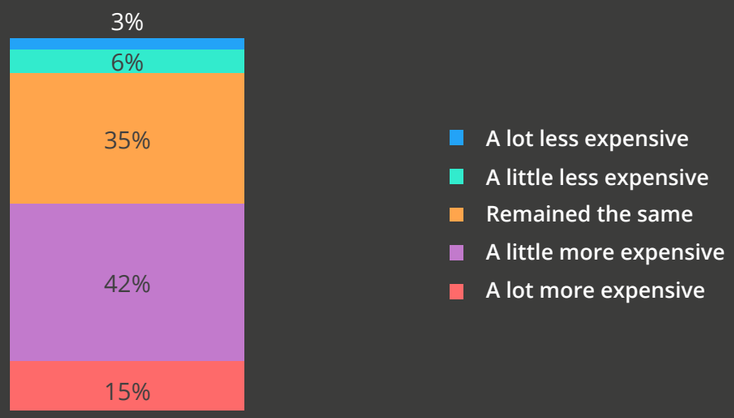
At present, eight in ten (77%) life sciences organisations say the increased costs of running clinical trials are being offset by savings made as a consequence of COVID-19, such as reduced overseas travel, and reduced attendance at congresses and conferences.

Life science organisations say that, since the start of the pandemic, there has been in increase in the time (49%) and the cost (57%) for completing a clinical trial. 188 billion USD was spent on R&D in 2020.

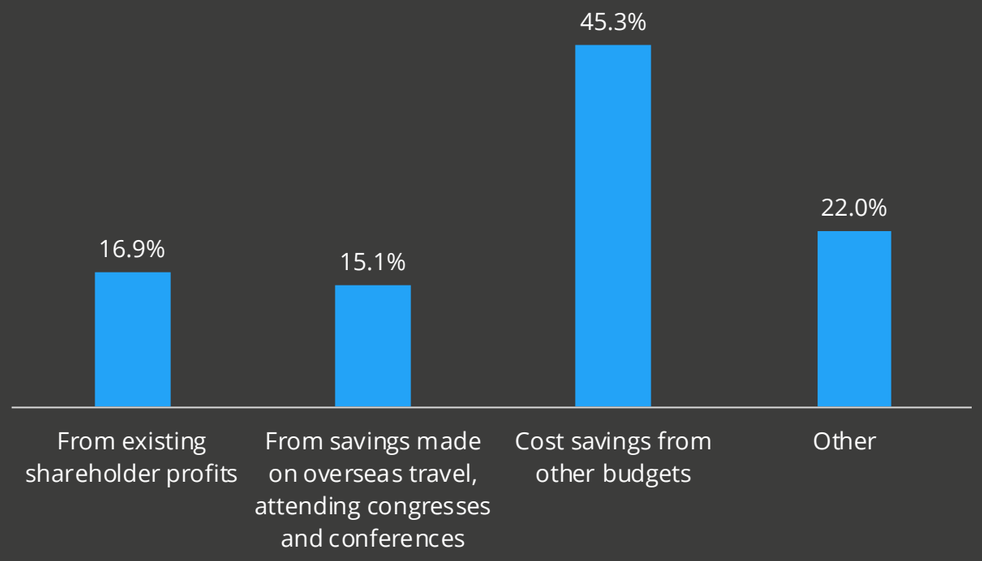
Since the start of the pandemic, in your opinion, how much has the time for completion of a clinical trial increased or decreased?



Since the start of the pandemic, in your opinion, to what extent have clinical trials become more or less expensive to conduct?



Eight in ten (77%) life sciences organisations say the increased cost of running clinical trials will be offset by savings made as a consequence of COVID-19, such as reduced overseas travel, and reduced attendance at congresses and conferences.



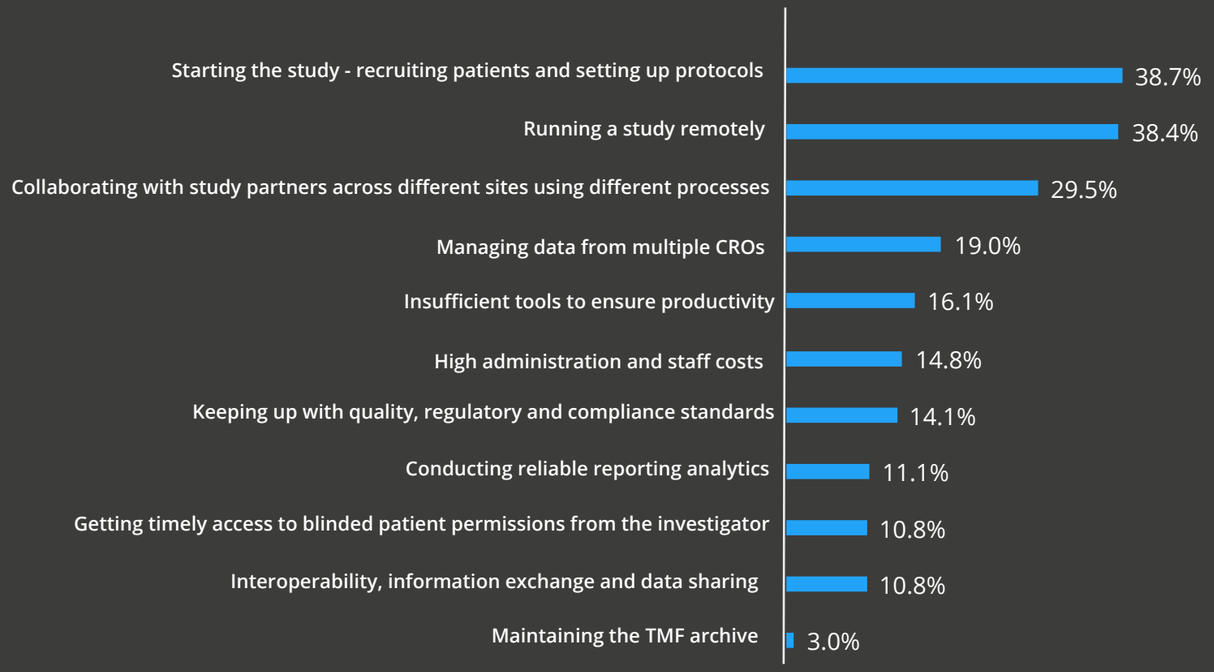
ii. Digital transformation: Kick-starting clinical trials to 'come back stronger'

Prior to the pandemic, an important area of focus for the life sciences industry was the adoption of technology to transform R&D, including clinical trials. Even in 2018, 86% of trials did not meet enrolment deadlines, and nearly a third of Phase III trials failed through an inability to recruit patients.[20] In 2021, the majority (90%) of life sciences organisations continue to face challenges when running clinical trials, from recruiting patients and setting up protocols to managing data from multiple CROs.

One third of all respondents confirmed that, over the next 12 months, their organisation will make a priority of adopting new technology (such as AI, machine learning and cloud computing) to aid the conduct of clinical trials and the management of trial data. All in all, some eight in ten (75%) life sciences organisations plan to invest significantly in technology. As transformation moves firmly up the board agenda, seven in ten organisations (70%) are likely to make a large investment in technology to enable interrogation of clinical data on a large scale. The aim is to further scientific discovery and meet regulatory requirements, while bringing down the cost and time it takes to conduct a clinical trial.

89% of all life science organisations face challenges when running clinical trials.

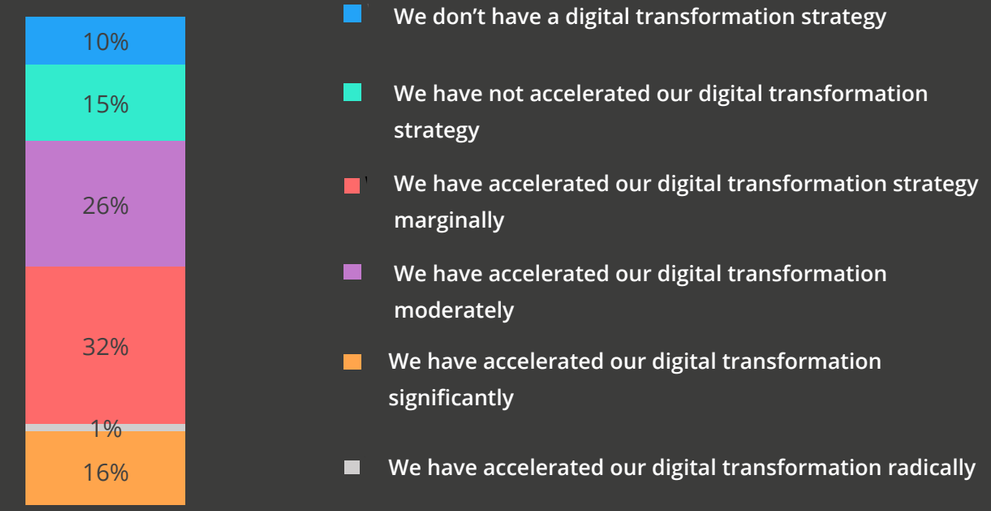
Which of the following do you find a particular challenge when running a clinical trial?



As a consequence of the pandemic 75% of life sciences organisations have accelerated their digital transformation strategies – adopting new technology to improve efficiencies.

As transformation moves firmly up the board agenda, seven in ten organisations (70%) are likely to make a large investment in technology to enable interrogation of clinical data on a large scale, with the aim of furthering scientific discovery.

As a consequence of the pandemic, has your organisation accelerated its digital transformation strategy?



Over the next 12 months, how likely is your organisation to make a large financial investment in technology to enable interrogation of clinical data on a large scale, with the aim of furthering scientific discovery?

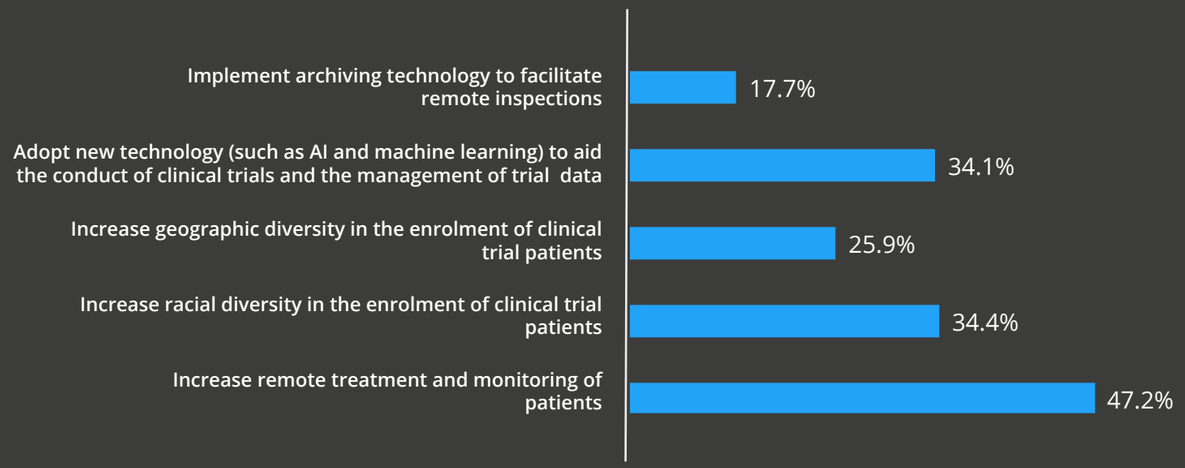
In 2021, the majority of respondents say that the pandemic presents an opportunity for changing the way clinical trials are conducted in the future. Two out of three (65%) life sciences professionals say that it is extremely or very likely that regulators will allow the decentralisation of clinical trials post-pandemic, and that they will continue to run trials remotely.

As the life sciences sector embraces new strategies to improve the way clinical trials are conducted, the priorities for clinical trials are to:

- Continue the decentralisation of clinical trials – increase remote treatment and monitoring of patients (47%).
- Increase racial diversity (34%) and geographic reach (26%) in enrolment of clinical trial patients.
- Adopt new technology such as AI, machine learning and cloud computing to aid the conduct of trials and the management of data (34%).
- Implement archiving technology to facilitate remote inspections (18%). In the course of the pandemic, remote inspections have become acceptable under certain circumstances. This interim measure is likely to become standard practice over the coming years, and to be formally integrated into regulatory guidelines.[21] In this evolving context, any archive that is not fit for the purpose of a remote inspection will come to represent a regulatory liability.

Over the course of 2020 the industry pivoted towards digital technology in a bid to overcome disruption to clinical trials and in order to continue treatment for patients. Consequently, two thirds (65%) of the life sciences sector say they will continue to run trials remotely post-pandemic.

As organisations look to improve the way they conduct clinical trials, which of the following will be a priority for your organisation over the next 12 months?

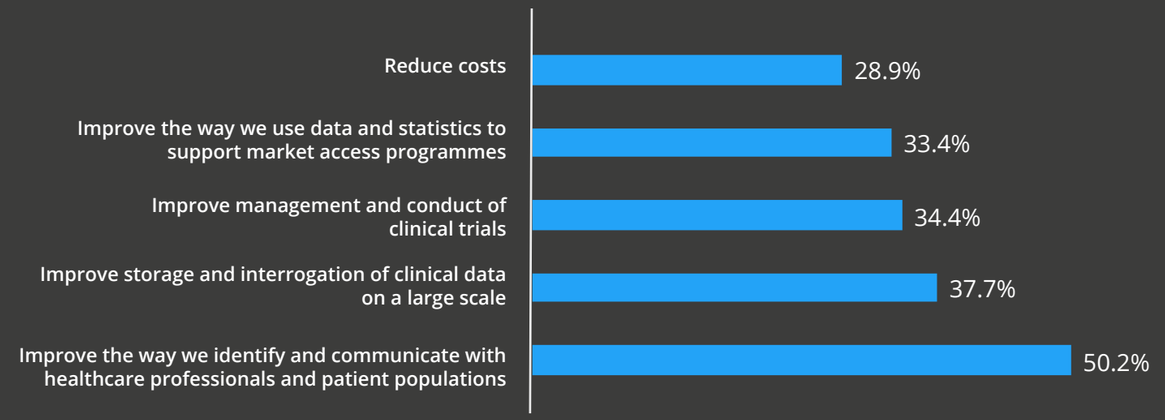


The survey findings suggest that digital transformation will serve primarily to:

- Improve the way the life sciences sector identifies and communicates with healthcare professionals and patient populations (cited by 50%);
- Improve archiving and integration of the eTMF and other data on a large scale (38%).
- Further the adoption of decentralised trials (34%).

50 per cent of digital transformation strategies are being driven by the desire to improve the way life sciences organisations identify and communicate with HCPs and patient populations.

What are the main priorities for your digital transformation strategy?



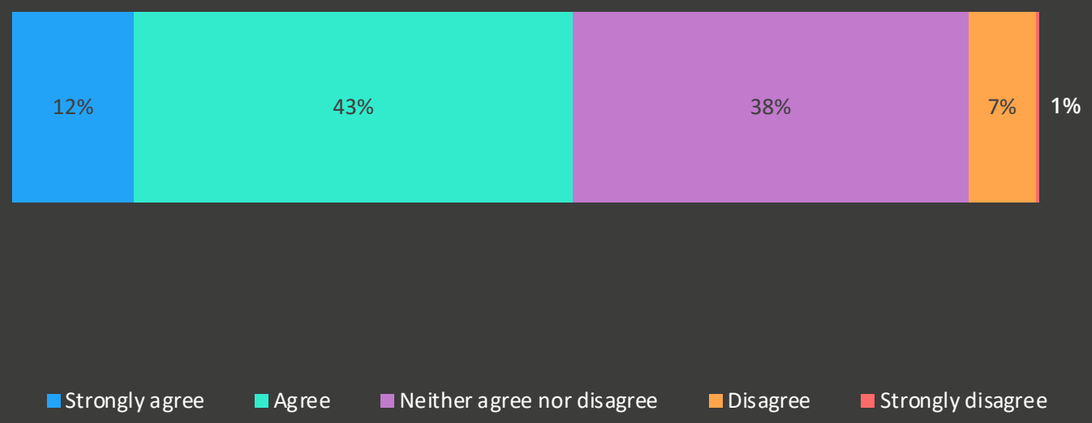
iii. TMF: Barriers to managing data and documents in clinical trials

The 2021 survey reaffirms another key finding of last year's TMF Futures report: the fragility of certain critical systems in the clinical trial process, notably a lack of interoperability between eClinical systems. Over half of life sciences organisations confirm that sub-optimal processes for data transfer from site investigators to the CRO and sponsor, and for storage, are potentially compromising the integrity and inspection-readiness of the eTMF.

Clearly, this can result in breaches of regulatory compliance, undermining progress that has been made and potentially causing delays to marketing authorisation applications (MAA). This comes at a time when the FDA plans to adopt electronic tools and when it is evaluating the disruptive impact of COVID on clinical trials – for instance on the quality of clinical data and the integrity of the trial.

55% of life science organisations say sub-optimal processes for data transfer from site investigators to the CRO and sponsor, and for storage, are compromising the integrity of the eTMF, resulting in breaches of regulatory compliance.

To what extent do you agree or disagree with the following statement? Sub-optimal processes for data transfer and storage from site investigators to the CRO and sponsor are compromising the integrity of the eTMF, resulting in breaches of regulatory compliance.



Over the last 10 years the quest to eliminate paper from clinical research – and thus increase efficiency, enhance collaboration and improve trial performance – has transformed the primarily paper trial master file (TMF) into an electronic trial master file (eTMF).

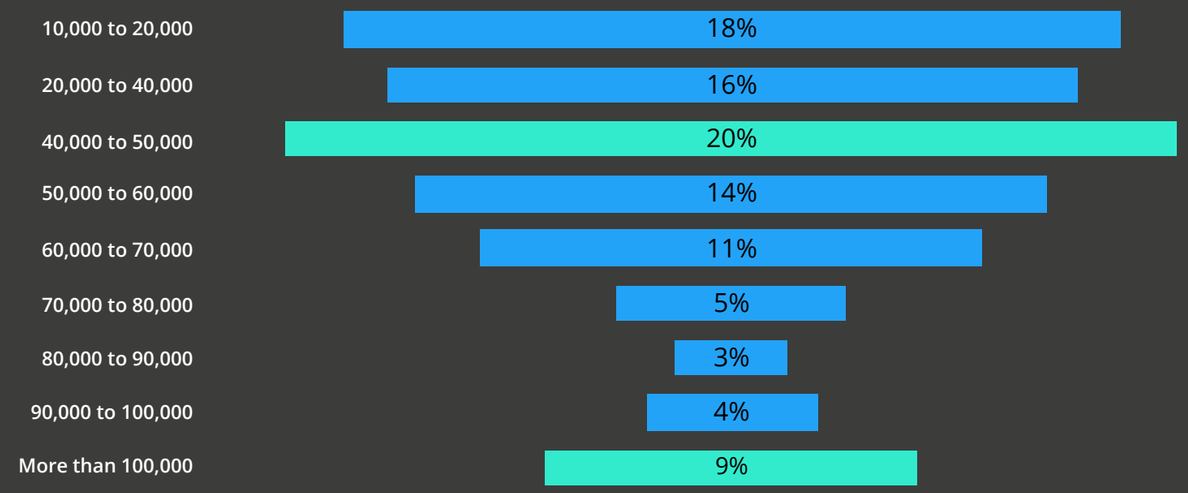
The survey finds that the eTMF is growing in complexity and size. This reflects an environment in which the number of complex clinical trials of new therapeutics, such as gene and cell therapies, is increasing. The average eTMF runs to 10,500 documents, yet 46% of eTMFs now comprise 50,000 documents or more; 9% of these comprise more than 100,000 documents.

As the eTMF grows in size and complexity, it becomes more important than ever to adopt technological solutions and management practices that are designed to streamline processes, assure integrity and maximise the security and interoperability of eTMF data at every stage of its extended lifecycle.

TMF: The eTMF is growing in complexity and size.

The average eTMF runs to 10,500 documents, but 20% of all eTMFs now comprise 40-50,000 documents and 46% comprise 50,000 documents or more.

How many pages and documents did your most recent TMF contain ?



iv. TMF Digital Archive: Meeting regulatory objectives

The eTMF has become the industry standard in the creation of the TMF, but the digital archive can provide the key to long-term inspection-readiness and unlocking the value of data.

Life sciences organisations operate in an environment in which data offers new possibilities, and which accords growing strategic weight to data management. That being said, the survey finds that less than half of respondents are using digital archives offering sufficient functionality to assure long-term inspection-readiness while also enhancing the sponsor organisation's ability to innovate, satisfy its commercial demands and meet its objectives.

When it comes to (digital) archiving, the survey suggests that substantial progress can still be made in terms of maintaining a secure archive which offers sufficient functionality both to:

i. Ensure long-term inspection-readiness (while remote inspections are becoming accepted practice, only 18% of respondent organisations are currently prioritising the implementation of archiving technology to facilitate them), and

ii. Enhance potential for extending the lifecycle and commercial potential of approved medicines (for instance through new indications and formulations, or licensing and partnership opportunities).

In light of this, it becomes questionable whether current archiving practice across the sector consistently conforms with the ALCOA+ and FAIR principles of data management or with the EMA's stipulation in its 2018 TMF guidance that "The dynamic character of the audit trail should be preserved, when applicable."

Nearly all (90%) life sciences organisations responding to the survey have a digital archive, but substantially fewer have an archive that is fit for purpose: 30% of all respondents and 80% of regulatory and compliance professionals describe their TMF archive as very or extremely inadequate.

Most confirm that their archives are NOT able to:

- Keep their data secure, accessible, and inspection-ready for 25 years (59%).
- Conduct searches in real time to locate files in seconds (66%).
- Handle large volumes of data (75%).
- Upload date from multiple sources (81%).
- Provide a clear audit trail (83%).

In 2014, the MHRA ruled that a deficiency in TMF could be classed as a critical finding in an inspection.[19] Since then, inspectors have been asking more questions about TMF – and also about archiving. Just half (48%) of life science organisations say that, if they were inspected tomorrow by a regulator, they would be extremely or very confident their eTMF would pass an inspection.

Among the main barriers to adopting an eTMF archive that can keep data secure, accessible and usable for 25 years (as stipulated by the EMA) are:

- The high cost of managing and storing data (37%).
- Incompatibility with existing software (36%).
- The attitude of the board, which does not view archiving as a priority (26%).

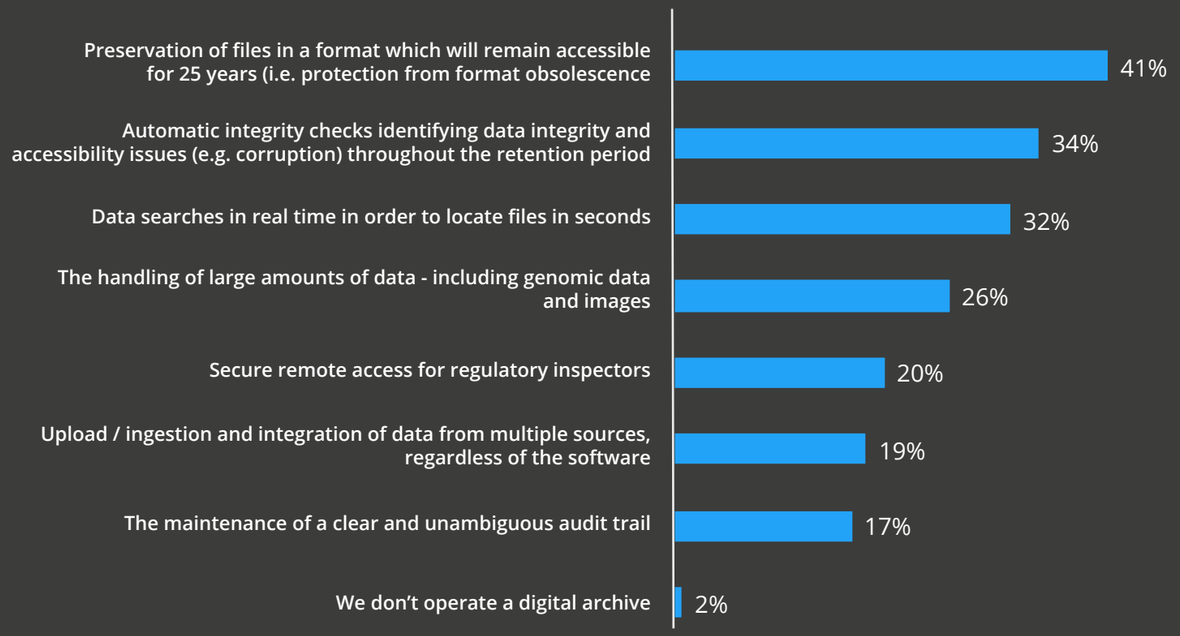
Stakeholders in clinical trials will benefit from surmounting the current challenges of interoperability and deficiencies in data management. There is also an opportunity to address the issue of archiving, and of good archiving practice, at an earlier stage in the clinical trial process.

Currently, just 33% of organisations make plans for the TMF archive at the pre-clinical stage or at study start-up at phase I. This does not conform fully with Good Clinical Practice (GCP) or favour the secure preservation of data in an inspection-ready condition for 25 years (EMA), and explicitly in accordance with the FAIR principles (Findable, Accessible, Interoperable, Reusable).

Maintenance of the TMF archive is often driven by regulation – the FDA and EU directives state that the TMF archive must be maintained for 25 years.

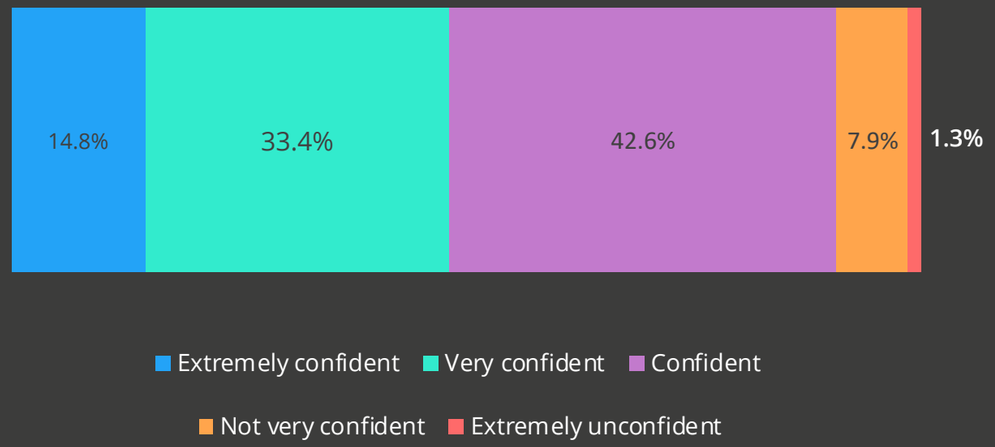
- **59% of life sciences organisations say they cannot guarantee that their eTMF archive will keep their data secure, accessible, and usable for 25 years.**
- **Few archives currently offer sufficient sophistication to meet the needs of the life sciences sector.**

Which of the following is ensured by your TMF archive?



In 2014, the MHRA ruled that a deficiency in TMF could be classed as a critical finding in an inspection. Since then, inspectors have been asking more questions about TMF – and also about archiving.

If you were inspected tomorrow by a regulator, how confident are you that your eTMF/TMF would pass an inspection?



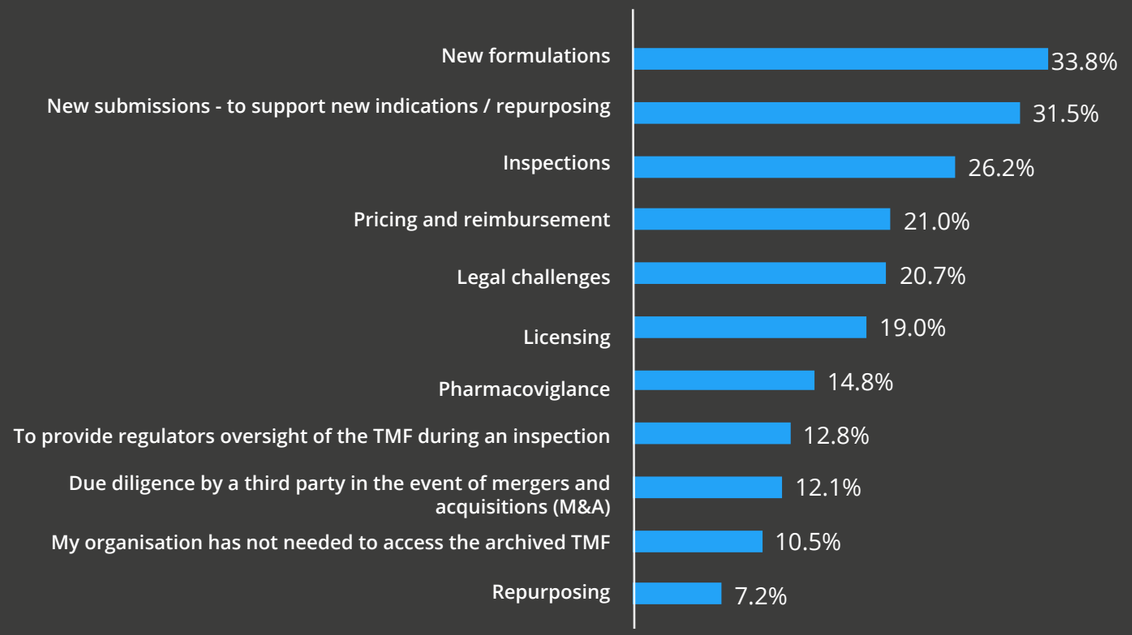
v. TMF: The living archive

In an operating environment marked by transformation and acceleration, the eTMF holds significant potential beyond its fundamental regulatory role. Living data in the eTMF archive is also playing an increasingly important role in extending the applications of certain treatments.

One in four (26%) life sciences organisations access the eTMF archive to support an investigation, or to provide regulatory oversight, but many access the archive either to support the extension of the lifecycle of a drug, or to meet broader commercial objectives.

Reasons for accessing the archive go beyond compliance: access is also needed for matters of patient safety, extension of drug lifecycles, and, increasingly, the provision of data for application in commercial issues such as legal challenges, licensing, and due diligence for multi-million/billion mergers and acquisitions.

Over the last year, why have you needed to access the TMF archive?



The life sciences sector is waking up to the true long-term value of data, and the archive now stores data other than the eTMF, including patient data (62%), lab data (40%) and genomic data (20%). The storage of this data also holds implications for compliance.

The fundamental purpose of the digital archive is to hold the eTMF, and keep it ready for regulatory inspection for up to 25 years (as per EMA guidelines). Now, as digital transformation gains further momentum, the life sciences sector is waking up to the true long-term value of its data. The 2021 TMF Futures survey respondents confirm that the archive now stores data other than the eTMF, including patient data (62%), lab data (40%) and genomic data (20%).

In the fight against COVID-19 a strategically informed approach to the collection, storage and sharing of data has produced enormous benefits.[9] Meanwhile, the UK debacle resulting from the use of outdated and inadequate spreadsheets highlighted the importance of keeping data alive in accordance with rigorous good practice.

'Data for Better Lives',[21] the World Bank's latest World Development Report, examines data's huge potential for doing good and laments the multitude of opportunities lost through weak statistical infrastructure.

Central to good practice in data management are the FAIR data principles, which assert that data should be Findable, Accessible, Interoperable, and Re-usable[16,17]. Complementing FAIR in such areas as pharmaceutical research, in which data integrity is of the essence, is ALCOA+:
An archive that stores eTMF and other important data from clinical trials should be designed and managed in accordance with both FAIR and ALCOA+ if it is to fulfil its various missions: to maintain the integrity of its contents in the long term; to ensure constant inspection-readiness and other forms of regulatory compliance, and to aid the life sciences sector in realising the full commercial and societal potential of its expertise and research.

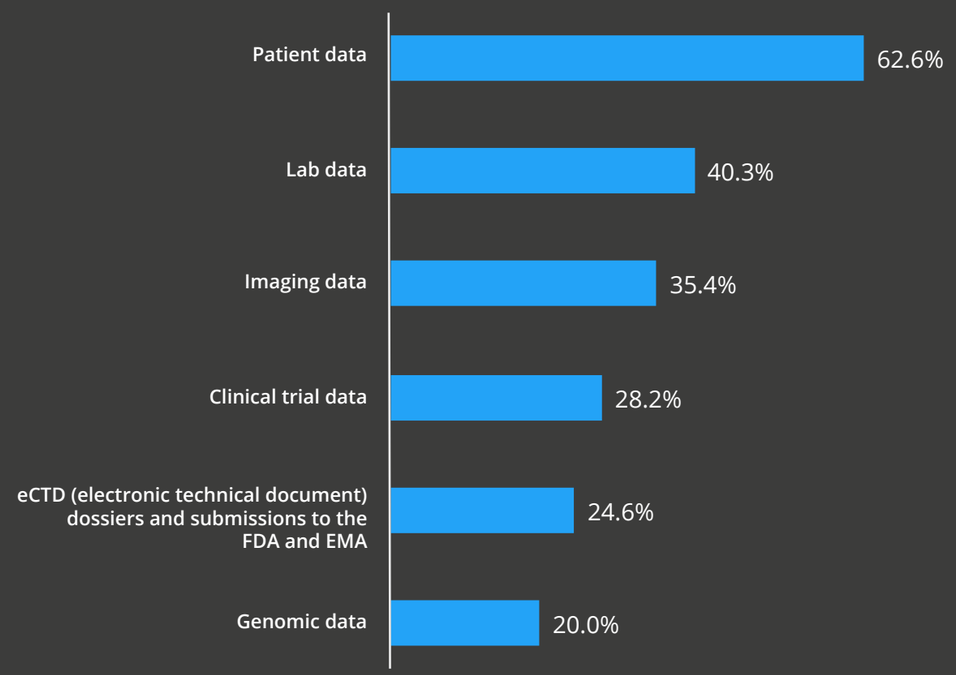
ALCOA	+
ATTRIBUTABLE LEGIBLE CONTEMPORANEOUS ORIGINAL ACCURATE	COMPLETE CONSISTENT ENDURING AVAILABLE

Just one of the many lessons learned from the crisis of the COVID-19 pandemic is that technology, beyond enabling business continuity, can rapidly prove transformative. Over the past 20 years, the power of data to empower discovery, drive business and shape our society has been proven time and time, again.

Once the crisis of the pandemic has passed, life sciences organisations, through their continuing investment in technology, can focus still more closely on making optimum use of high-quality, rigorously organised data. It will play a central and multi-faceted role in reducing the cost of developing new therapies, bringing them to market more quickly and, through innovative thinking and practice, maximising commercial and societal benefits at every stage of the extended product lifecycle.

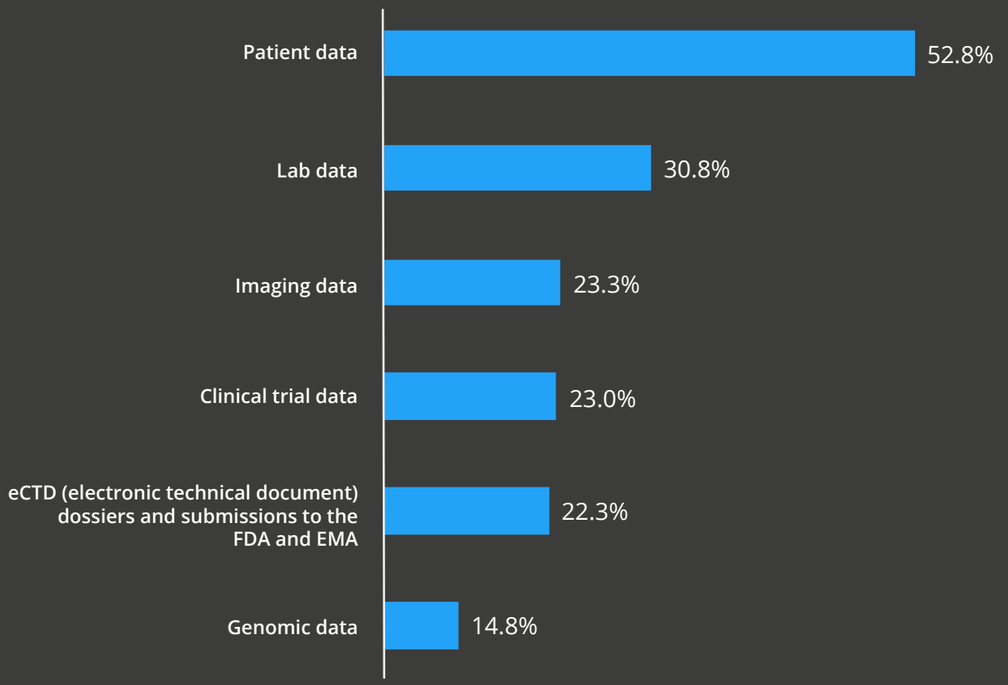
The life sciences sector is waking up to the value of data, and the archive now stores data other than the eTMF.

In addition to the eTMF what other types of clinical trial data do you archive?



As the importance of data grows, so does the risk if it is not archived correctly.

Which of the following data poses the greatest risk to your organisation if not archived correctly?



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About Arkivum

Arkivum is recognised internationally for its expertise in the archiving and digital preservation of valuable data and digitised assets in large volumes and multiple formats. The long-term security, integrity and accessibility of data is crucial for all Arkivum's clients and partners, who share a commitment to good practice in its stewardship and governance.

Arkivum's specialist software and services are chosen by major institutions and commercial organisations in a diversity of sectors, including life sciences, research (CERN), financial services, and organisations in higher education, culture and heritage. Confident in Arkivum's reputation and resources, they are in a position to maximise insight and discovery by deriving optimum long-term value from their data, collections and intellectual property.

Headquartered in the UK, with presence in the US, Arkivum advocates the use of the FAIR principles in data management: Findable, Accessible, Interoperable, Reusable. Arkivum is also certified in ISO 9001 and 27001.

For more information about the product, or to arrange a demo, please email us on hello@arkivum.com or visit www.arkivum.com

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