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21st Century Clinical Trials
Cloud-Based Quality & Compliance

Your Presenters

Paul Fenton
President & CEO

- 15 years experience in the implementation of technology for clinical trials
- Involved in various initiatives for development of standards and models for regulated content management
- Regular industry speaker on technology
- Auditor in clinical systems and processes

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Your Presenters

Frederic Landry
Director of Business Analytics & Operations

- Operations and production professional with over 15 years of experience
- Extensive industry experience in quality management, system design, project management and process improvement
- Passion for combining industry knowledge, business mechanics and existing technologies

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Webinar Series

- Aims to look at technological trends and new organizational models in clinical trials
- Special focus on cloud based solutions
- Participants should gain a good grounding on how these technologies are enabling change in how we work
- The webinars aim to be practical also and give you criteria and decision making tools to implement technology and change
- For more info go to: www.montrium.com/webinars

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Housekeeping

- Slides can be distributed upon request. Details on how to request slides will be distributed to attendees following the webinar
- Details on the **next webinar** will also be distributed
- Feel free to ask questions in the **questions panel**
- You can also **Tweet** me at **@paulkfenton**
- Thank you for your interest!

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Agenda

- Overview of new organizational models in clinical R&D
- Virtual quality assurance oversight
- Centralized procedures
- Cloud based quality events management
- Quality metrics and reporting
- Cloud-Based QMS
- Opportunities for the future

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Overview of new organizational models in clinical R&D

1

The good old days

- In the past, **clinical R&D** was typically conducted by **individual** organizations or CROs
- Organizational structures were **less distributed** and **fewer** development partners were **involved**
- Each group would manage their own **processes, QA oversight** and **quality records** with few shared or cross-organizational procedures
- **Budgets** were not such an issue and **compounds** were more **traditional**
- There was less focus on **QA and risk based approach** from the **regulators**

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The New Era in Clinical R&D

- Patent cliff
- Personalized medicine
- Need to do more with less
- The need to be more agile
- Ever increasing outsourcing of R&D activities
- Complexity and globalization of clinical R&D
- Increased scrutiny from regulators
- Clarity on expectations surrounding risk based approach from the regulators
- Stronger focus on quality, risk management and traceability from the regulators
- More technology and better technology

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New Organizational Models

- Clinical R&D is becoming decentralized and is being managed through networks of organizations
- These organizations each have their own specific area of expertise
- Collaborative technology plays an important enabling role in this model
- The model aims to be able to be more agile and focused while reducing cost and time to market
- This poses new challenges for the management of processes and quality….

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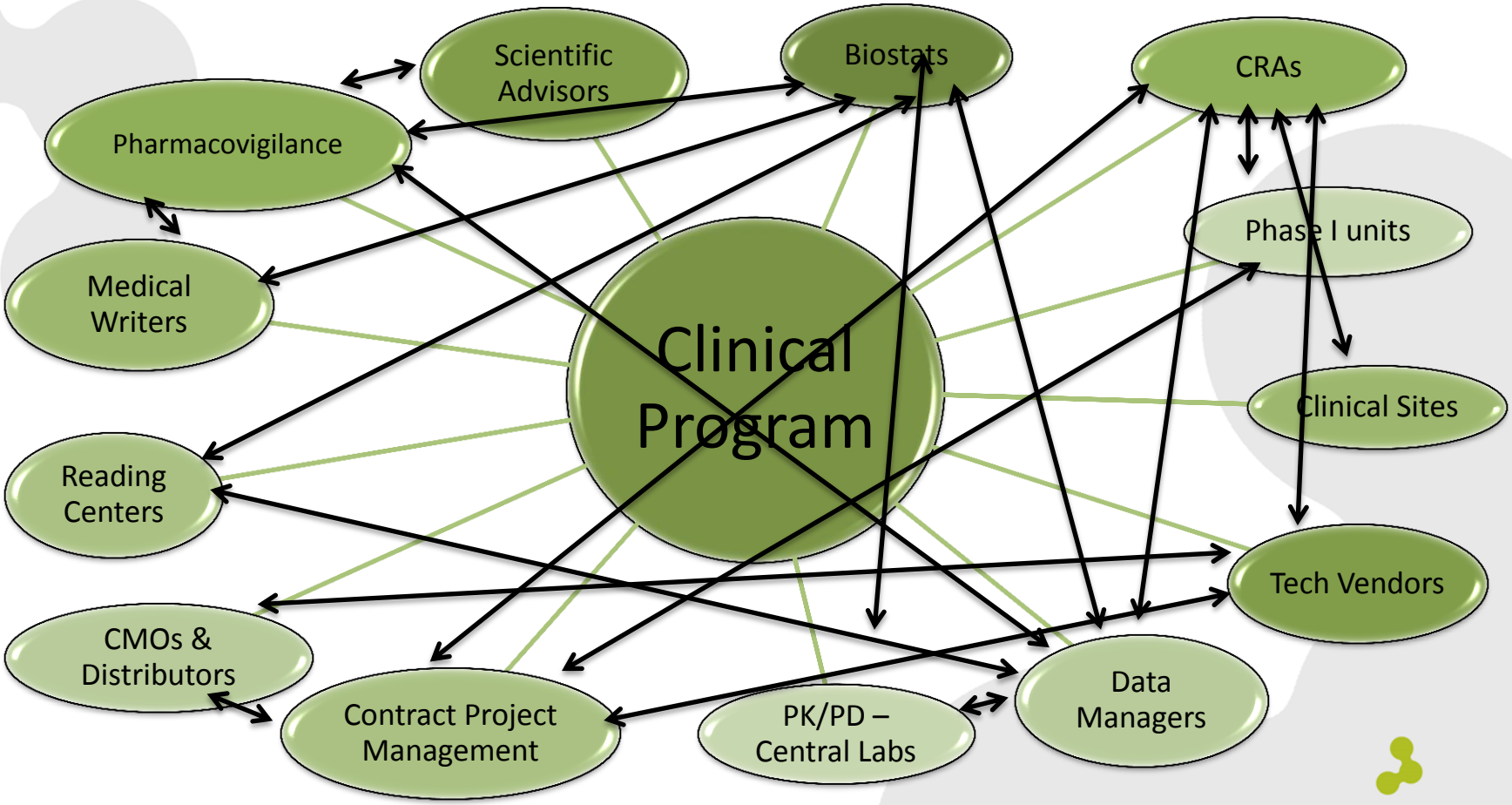
The New Organizational Network



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Virtual quality assurance oversight

2

Traditional Quality Management

- **Each organization** has its **own quality system** and quality oversight
- **Smaller organizations** typically work with quality **consultants**
- **Quality events** are managed **internally** unless they impact the sponsor
- Sponsors have to **periodically verify** that vendors have **adequate** procedures, documentation and quality **controls in place** and that they are **compliant**
- **Sponsors** remain **ultimately responsible** for quality and compliance
- **Sponsors** ultimately **pay** the costs associated with quality

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Challenges of the traditional system

- Processes which **span multiple organizations** need to be band-aided with **study specific** procedures and plans
- **High variability** in quality system structure, quality standards and interpretation of regulations
- **Audits** are time consuming, expensive and only represent a specific **snap-shot** in time
- Sponsors often **find out** about quality issues when it is **too late**
- Sponsors need **better** ways to **ensure regulatory compliance** and reduce **regulatory risk**
- Sponsors **tend to accept** each organizations procedures as it is too difficult to impose thier own procedures

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Networked Organizations need a new model because….

- Networked organizations:
  - Need to work together as one
  - May not have QA in house due to size
  - May not have procedures to accomplish the tasks required by the sponsor
  - Are more open to adopting centralized cross-organization procedures as an extension of the sponsor organization
  - Need an easy way to communicate quality issues and events to sponsors and partners in a timely manner

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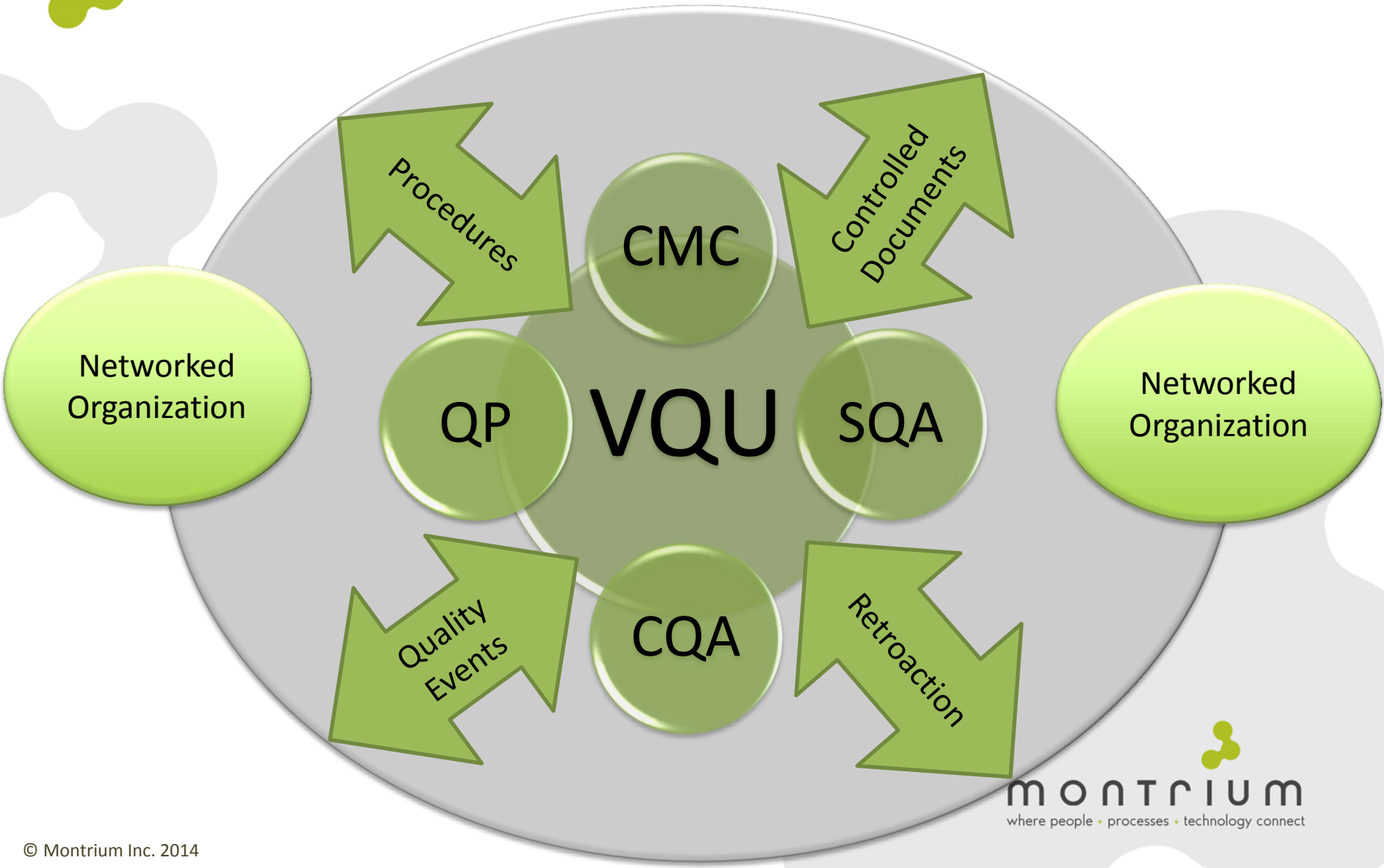
Enter - The Virtual Quality Unit



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A successful VQU

More than ever, a virtual quality unit:

- Takes a **collaborative** and **supportive** approach to quality assurance
- Lives within a culture of **quality ownership** from the individuals performing the work
- **Enables** and **facilitates** continuous improvement
- **Encourages** and **rewards** open communications and transparency
- Acts as a **central organizational, repository and communication hub** for quality management
- Works from and relies on **standardized processes**

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Centralizing Controlled Documents

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What is a Controlled Document?

- A document which, through the course of its lifecycle may be reviewed, modified and distributed several times.
- A document that ensures that we work in a systematic and controlled way.
- A documents going through a formal document change control process in order to be modified.
- Examples:
  - Procedural Documents (Policies, SOPs, WI, Forms and Templates)
  - Master Batch Record
  - Manufacturing Specifications
  - Test Methods

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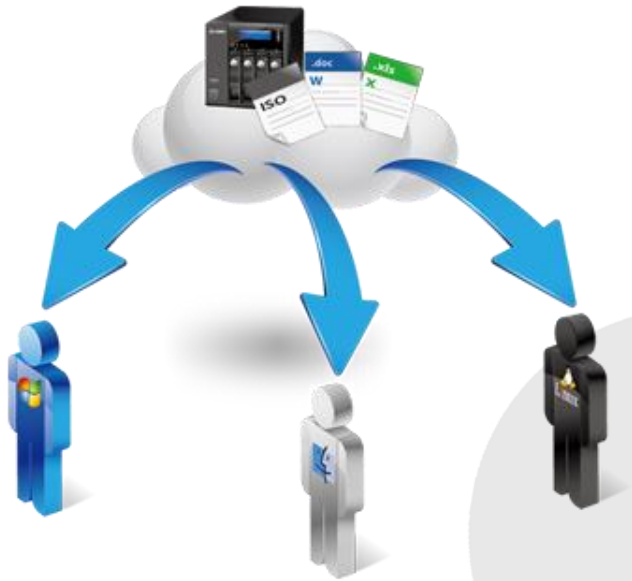
How are Procedures Managed Today?

- Most organizations have their own procedures and study specific plans
- In some instances sponsors will require organizations to follow sponsor procedures, which are distributed manually
- Many documents are also transmitted via emails or drop box type solutions



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Typical impacts associated with a decentralized system

- Changes are **complex**, **slow** and **prone to errors**
- **Local copies** make it difficult to ensure correct versions are used
- **Large investments** required by Sponsor to ensure adequacy of local procedures
- **Manual distribution** makes tracking difficult
- Changes cause **disruptions in cross-organizational processes and plans,** especially if changes are not adequately communicated
- Continuous improvement is stifled, keeping the overall system in a perpetual **reactive state**

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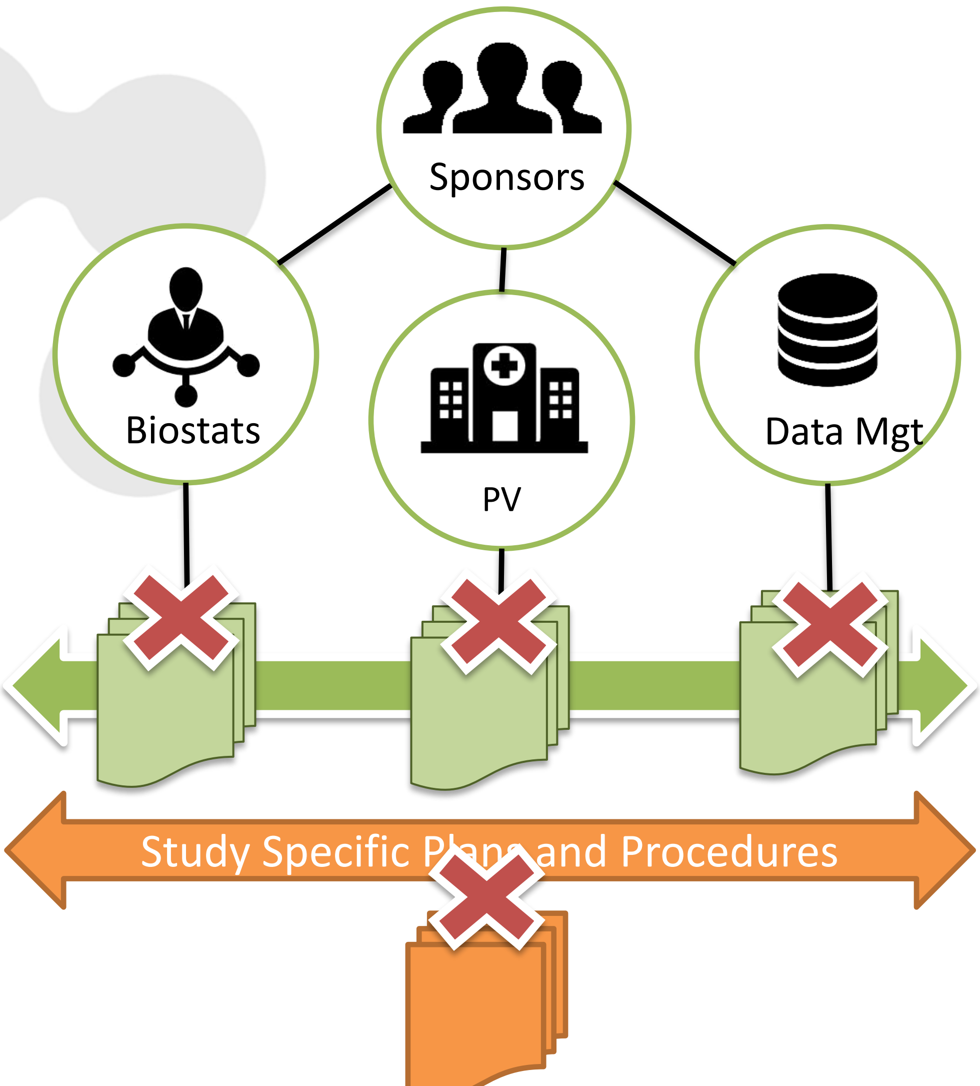
A Real Life Example



1 2 3 4 5 6

If sponsor was to put in place a cross org process, for the PV reconciliation across [illegible] information will be [illegible] activities that would impact DB lock.

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Centralizing Controlled Documents

Different levels of procedural documents must be managed:

- **Global Sponsor:** Under the complete responsibility of the sponsor, and with which the partner organizations must comply

  (e.g. Deviation Reporting SOP, SOP on SOPs)

- **Cross-organizational:** Defined in partnership with the organizations involved to support cross-organizational processes

  (e.g. PV Reconciliation, Management of Blinded Information)

- **Organization specific:** Defined and managed internally by the relevant organization(s) and stored within the centralized system

  (e.g. ECRF Set-Up, Biostatistical programming)

- **Clinical Program or Study Specific:** Governing program or study specific activities

  (e.g. Coding of Adverse Events, Management of Clinical Supplies)

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Advantages of Centralization

- Enhanced standardization
- Less redundancies
- Adaptability
- Enhanced collaboration within geographically dispersed teams
- Availability of information (anytime/anywhere)
- Environmentally friendly
- Less prone to error associated with changes = less rework
- Facilitates training
- Enhanced security
- Improved controls and traceability

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Challenges of centralized controlled documents

- Controlling printed copies
- Collecting signatures
- User access and security management
- Configuration management
- Training
- Technical support
- Managing cultural change
- Eliminating parallel systems and work-around
- Variability of organization's size and maturity
- System integration
- Maintaining a validated environment

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Cloud based quality events management

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Defining Quality Events

- Quality events primarily consist of **deviations** and **incidents** in clinical R&D
- Quality events should include attributes that are leveraged during monitoring and trending:
  - Source document (SOP, method, policy, etc.)
  - Criticality (critical, high, low)
  - Location (business unit, site, region,)
  - Governing document (policy, SOP, protocol, etc.)
  - Responsible Unit (business unit, department)
  - Status (reported, analysed, resolved, close)
  - Etc.

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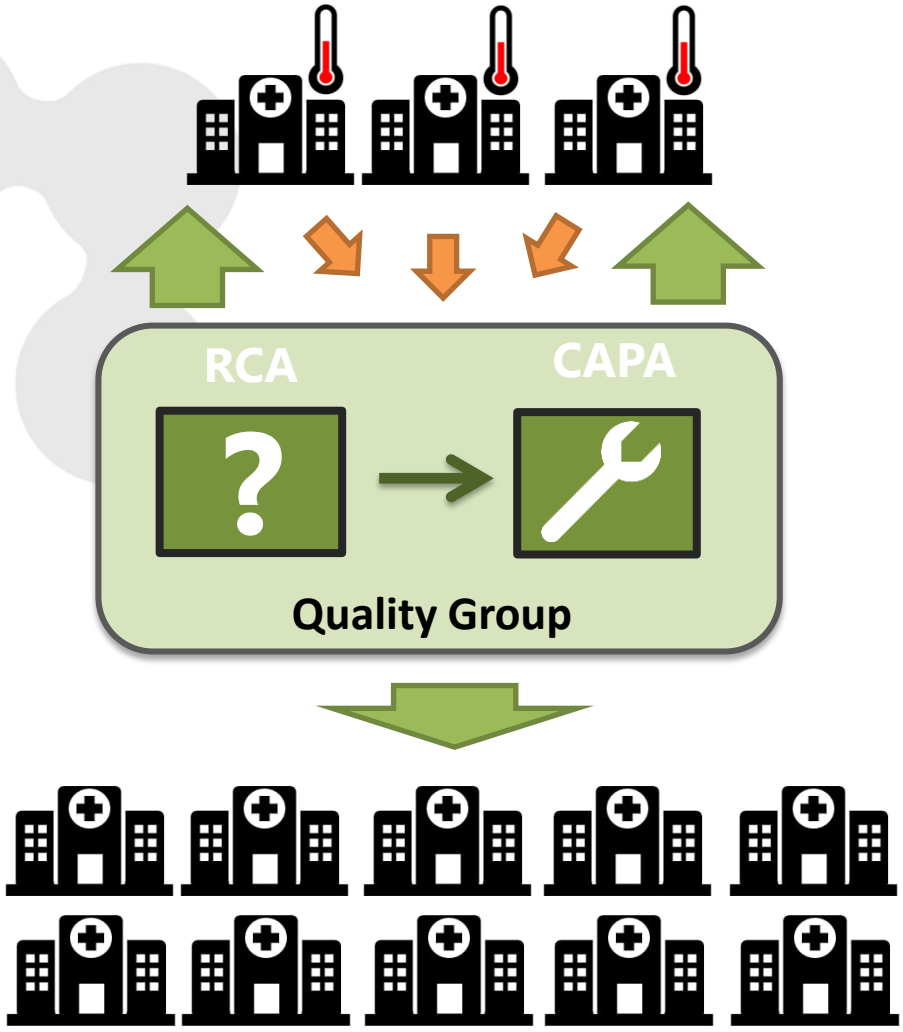
Quality Event Management Example



1. High number of temperature deviations reported at 3 clinical sites for a specific study
2. Events are centrally monitored and analyzed (RCA)
3. The RCA effort concludes that the IMP storage instructions are not clear, requiring updates, redistribution, re-training
4. Actions are implemented at reported sites, and also at all other sites in relevant studies and programs

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Handling Quality Events

- **Reported when** and **where they occur** by an **authorized** and **trained** individual
- **First analysed locally** by the responsible person or group to verify their validity and urgency
- **Layers of analysis/reviews** are possible based on various factors (e.g. organization structure, type and urgency of the event, etc.)
- Corrective/Preventive Actions are applied
- Associated actions and their impacts are **reviewed, monitored** and **trended centrally**
- Managed by following **standardized processes**

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Pre-requisites to Event Based Management in the Cloud

- Consistency of reported format and classification of events:
  - Central forms
  - Training
  - Standardized processes
- Clearly defined quality management structure with no gap or redundancies of responsibilities

Quality metrics and reporting

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Why do we need metrics?

- Risk based approach to clinical trial management
- Business intelligence (aka operational insights)
- Feeding quality trend and events into other clinical operations processes (e.g. clinical site monitoring)
- Retroaction and improved planning and management of clinical trials
- Proactive approach to quality management

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Leveraging Quality Events

- Strong **industry** and **technical** knowledge must both be available
- **Industry knowledge** is required to:
  - Define how to **process** quality events
  - Identify **critical data** a system should capture,
  - Identify the **key questions** a QMS must answer
- **Technical knowledge** is required to:
  - **Design** and **build** a system that can ensure process **standardization**, **capture** of critical data, and the ability to quickly **provide answers** to the key questions

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Information or Data Focus?

- Data System supports primarily **add-hoc reporting** with minimal reusability.
  "We don't know what to capture, so we capture almost everything."
  "Why am I entering all this information?"

- Information system supports primarily **live dashboards** providing real-time organizational insights.
  "I can find the answers I need so much faster!
  "I didn't think this change would have such an impact!"

Information systems hold purposeful data. Is your system Business Intelligent?

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Cloud-Based QMS

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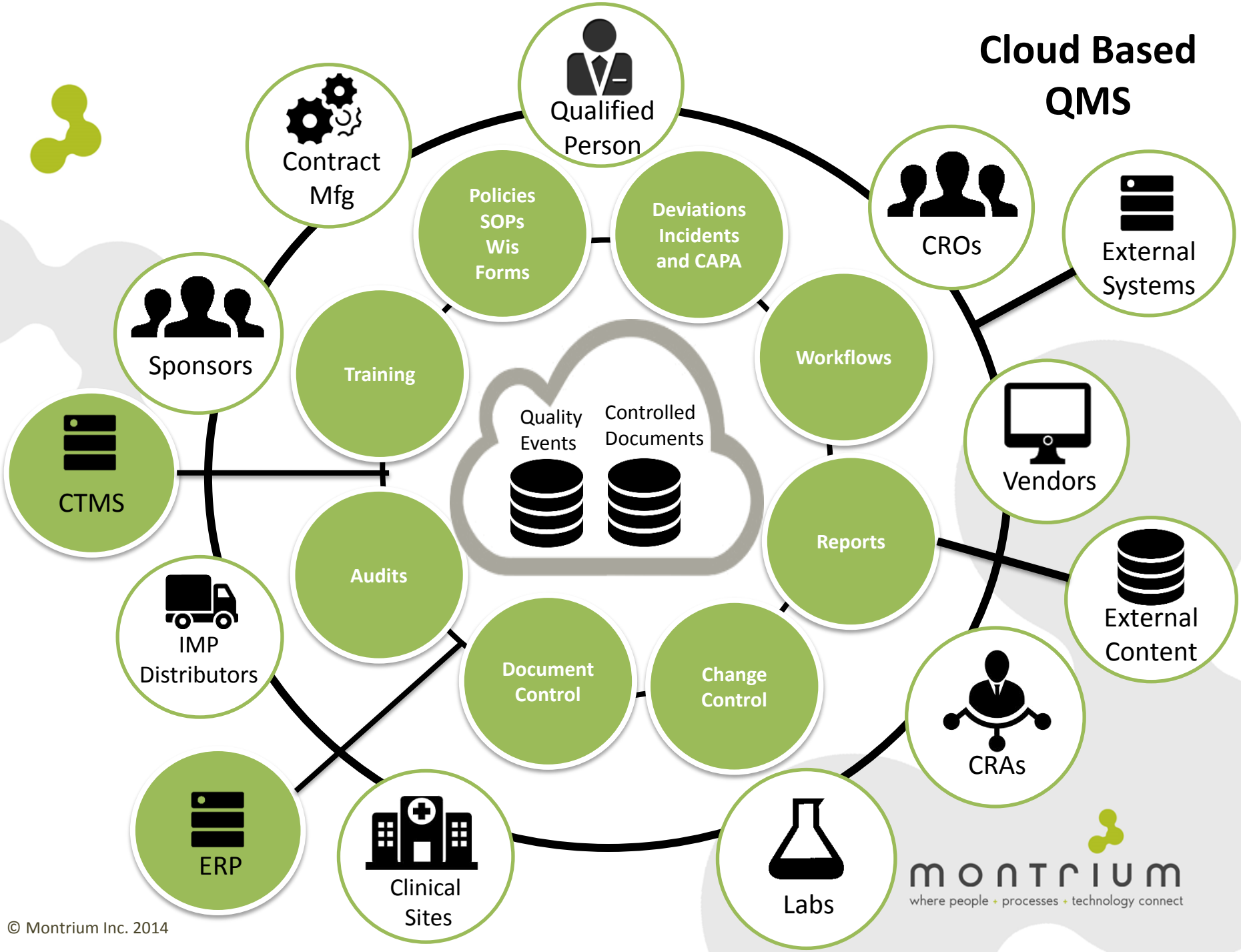
Cloud Based QMS



Questions to ask yourself before moving to a Cloud-Based QMS?

- Who will need to interact with your quality system?
- What quality activities will be managed in your quality system?
- Do you need a customized or OOTB solution?
- What is your budget?
- Do you have the required procedural controls and knowledge to deploy and manage a validated QMS?

http://blog.montrium.com/blog/5-questions-every-company-should-ask-themselves-before-selecting-an-eqms

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Opportunities for the future

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Opportunities for the future

- Centralized virtual QP for product release
  - In Europe an independent QP (Qualified Person) is required to release a batch of product
  - In the US the product owner must be responsible for this
  - If manufacturing is outsourced, then the product owner cannot rely on the manufacturing facilities internal QA
  - Relevant batch records and CoAs could be loaded into the central environment
  - An independent QP could then review the documentation on the central platform and virtually release the product
  - This is acceptable as long as the sponsor / product owner contracts the QP

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Opportunities for the future

- Risk-Based Clinical Trials
  - There is a clear expectation from the regulators that we apply a risk based approach to all activities within a clinical trial
  - There are also benefits for the sponsor
  - Quality event data can provide valuable insights especially when combined with other operational and clinical data
  - This data can be transformed into knowledge and used to detect potential risks and also be used for planning for risk based activities
  - Having centralized, standardized quality event management exponentially enhances this approach

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Opportunities for the future

- Improved traceability, inspection readiness and remote auditing:
  - Centralizing the quality system allows us to have a much better overview of all quality events and activities across a clinical trial or program
  - This would have a positive impact during inspections as it would be easier to trace events and access information
  - Fewer audits would also be required if we were able to centralize procedures and quality events and remote for cause audits could be conducted online

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Next Webinar…

21st Century Clinical Trials

Qualified Cloud Strategy

Date: December 11th, 2014

Time: 8am PST / 11am EST / 5pm CET

Where: www.montrium.com/webinars

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