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STATISTICAL SOFTWARE & SERVICES

Secure Interim Analysis Data Access and Automated DMC/DSMB Management with ACES[®]

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Introductions: Today's Speakers



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What You Will Learn



- The considerations when forming information paths for DMC/DSMB communications
- Scheduling an interim analysis – when is best?
- How to build firewalls to protect interim data
- What can you do to build regulatory trust?
- How to automate generation of supporting documentation needed for interim analysis
- How is ACES being used today?

Agenda



- Background
- Traditional Process Concerns
- DMC/DSMB Communications
- Planning Interim Analyses
- Where Does ACES[®] Fit In?
- Actual and Potential Benefits
- Closing Remarks
- Q&A

Background



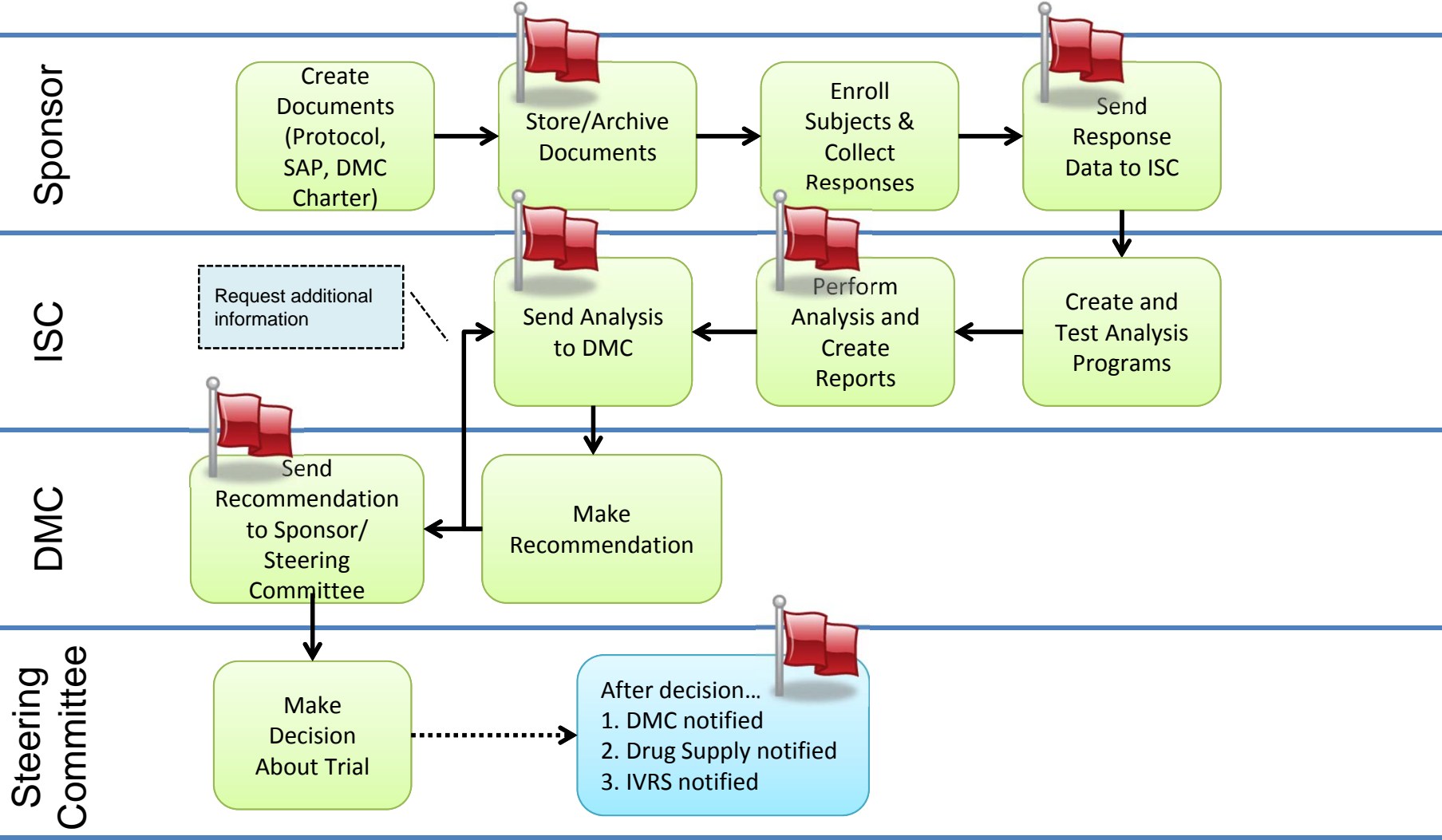
Over the past 10 years, there has been an significant increase in the use of Data Monitoring Committees.

- Safety monitoring is required
- Role of DMCs is expanding and becoming more complex
- Traditional DMC responsibilities
- Adaptive design clinical trials increase DMC responsibility
- Adaptive design requires a communication plan that allows for trial modifications after interim analyses

Key Roles in Interim Analyses

- Sponsor
- Independent Statistical Center (ISC)
- Data Monitoring Committee (DMC)
Data Monitoring Safety Board (DSMB)
- Steering Committee
- IVRS
- EDC
- Drug Supply

Traditional Process



Concerns with Traditional Process



- SOP Training and Enforcement
- Firewall Implementation
- Operational Bias
 - Unblinded Analyses
 - Blind Maintenance
 - Assurances of Limitation
 - Sponsor Involvement
 - Steering Committee Involvement
- Lack of Consistency
 - Process
 - Notifications
 - Snapshots
 - Interim Analyses Data
 - Analysis Programs
 - Output
 - Documentation
 - Who, What, When
- Security
 - Information Access
 - Lack of Auditing

How Can ACES Help?



ACES is a secure, web-based platform to help clinical teams implement fixed and adaptive trial designs with interim analyses



Workflow Automation



Secure Firewalls



Document Storage



Auditing



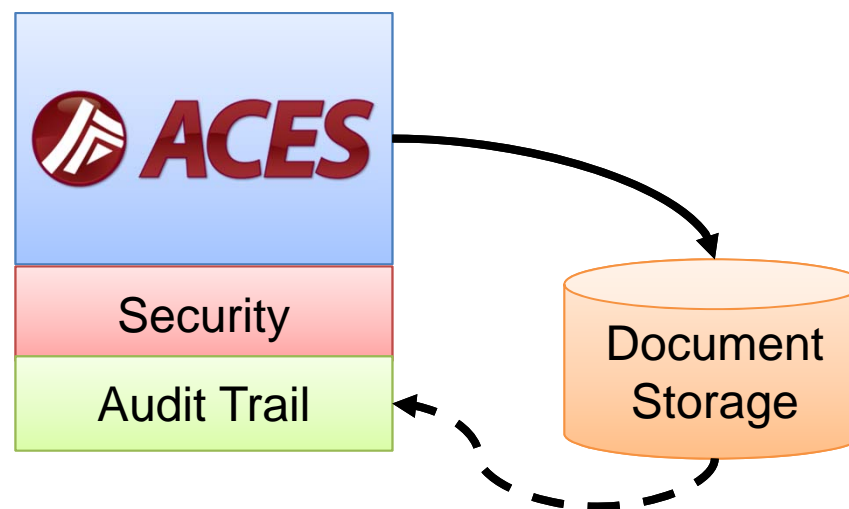
Reporting



Global Access

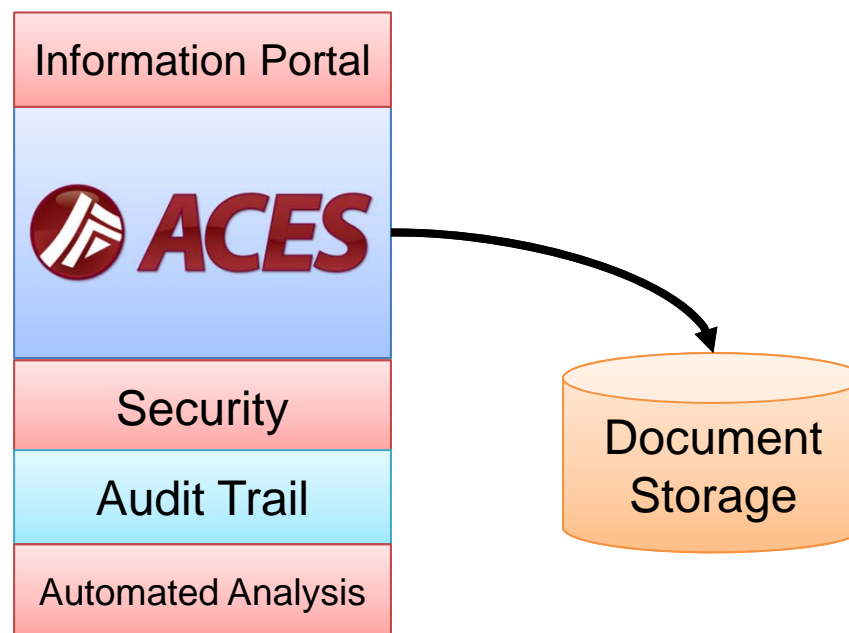
Protect Trial Integrity

- Create Secure Firewalls
 - Unique Usernames and Passwords
 - Role Based Security
 - Maintains Study Blind
- Document and Information Storage
 - Centralized
 - Controlled Access
 - Auditable

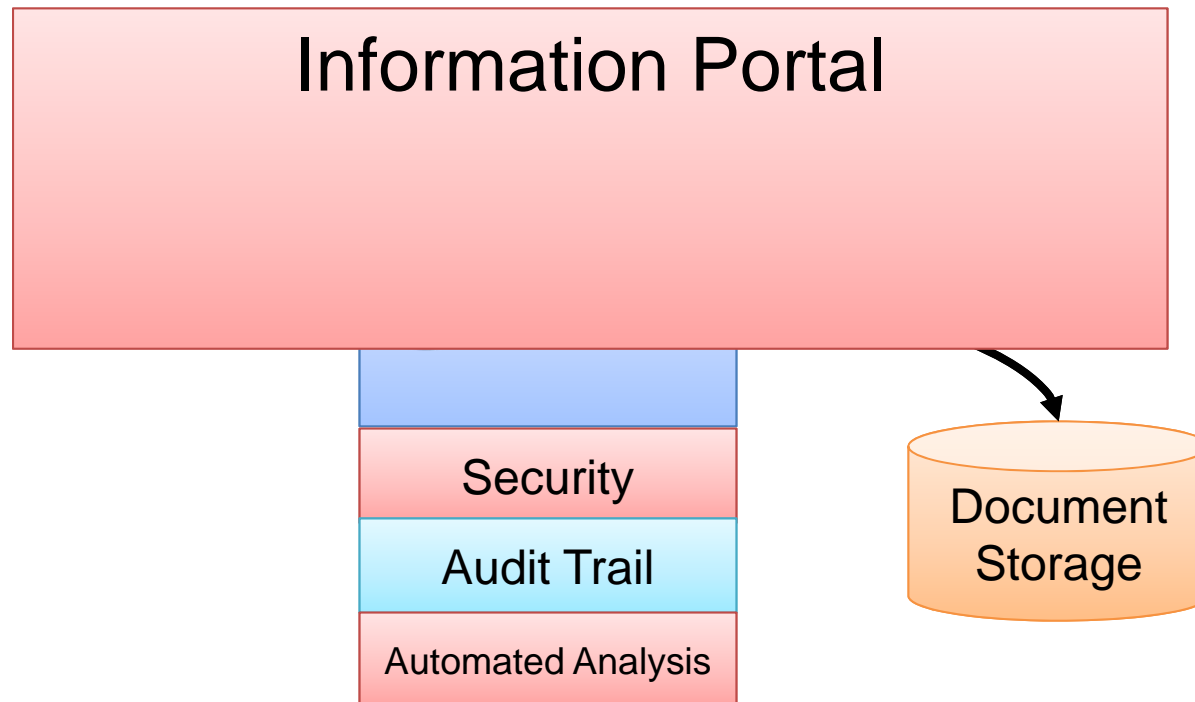


Reduce Operational Bias

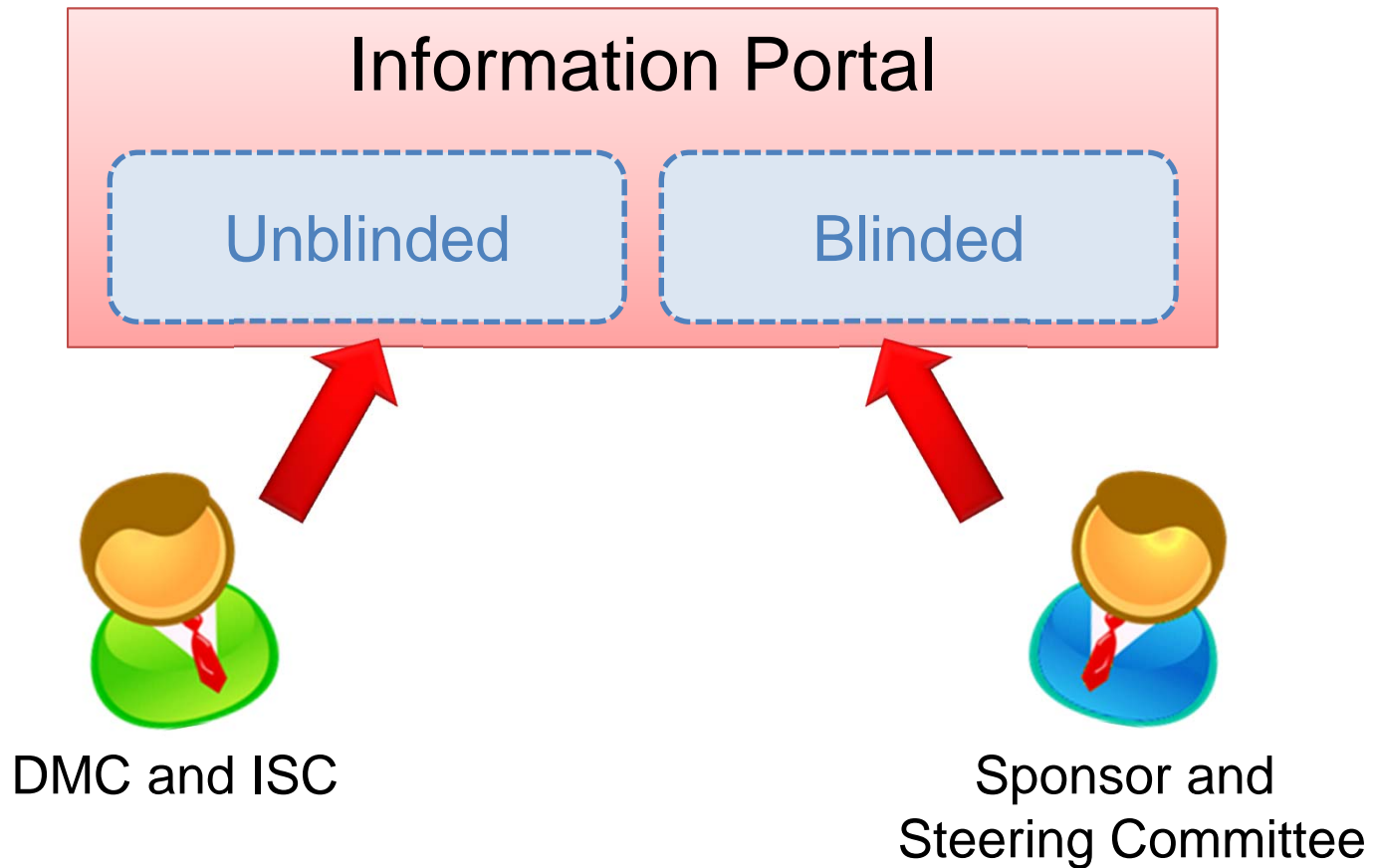
- Automated Analysis
 - Blinded Interim Analysis
- Restrict Access to Blinded Information
 - Limit Sponsor Involvement
- Control Access to Information
 - Centralized Information Portal



Firewalls



Firewalls



Building Firewalls and Protecting Data



- “Sponsor exposure to unblinded interim data, through the DMC or otherwise, can present substantial risk to the integrity of the trial.”
- “Unblinded interim data and the results of interim analyses should not be accessible by anyone other than DMC members or the statistician(s) performing these analyses and presenting them to the DMC.”
- “Sponsors should establish written procedures, which may be included in the DMC charter, to ensure the minimization of bias, such as maintaining confidentiality of the interim data.”

ACES satisfies these requirements by enforcing the rules identified in the DMC Charter, and by providing unequivocal evidence of that enforcement.

Source: FDA Guidance: Establishment and Operation of Clinical Trial Data Monitoring Committees, March 2006

Building Regulatory Trust



"A well-trusted firewall established for trial conduct **beyond those established for conventional group sequential trials** can help provide assurance that statistical and operational biases have not been introduced."

FDA Draft Guidance on Adaptive Design (2010)

Automating Analysis and Reporting

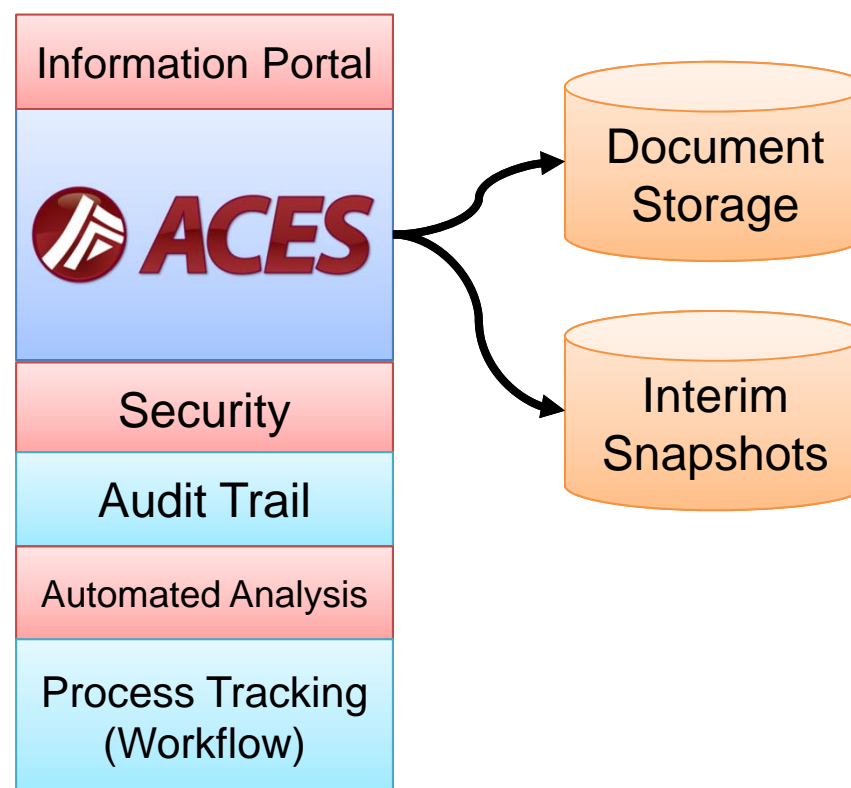
- FDA recommends that the DMC or the group preparing the confidential interim reports to the DMC maintain all meeting records in order to best ensure continued confidentiality of interim data.
- FDA may request copies of these records when the study is completed.
- FDA may also request access to the electronic data sets used for each set of interim analysis.
- FDA recommends that sponsors arrange for archiving such electronic data sets.

ACES satisfies these requirements providing capabilities to automate interim analysis reporting, archive input data sets and output reports, and maintain meeting records.

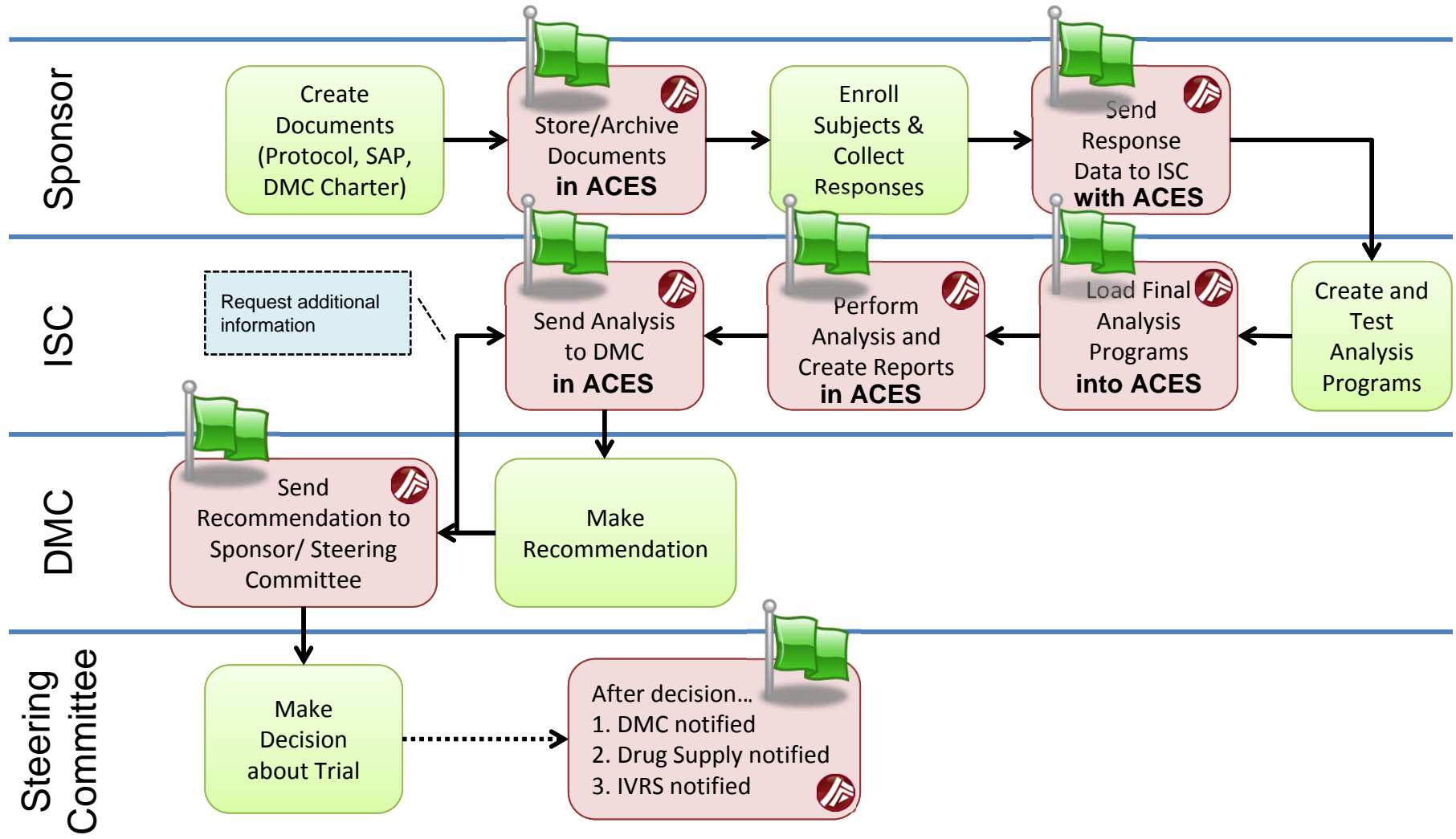
Source: FDA Guidance: Establishment and Operation of Clinical Trial Data Monitoring Committees, March 2006

Increase Regulatory Trust

- Auditing
- Accountability
- Automatic Snapshots
 - Data
 - Parameters
 - Outputs
 - Decisions
- Real-Time Process Inspections
- Consistency



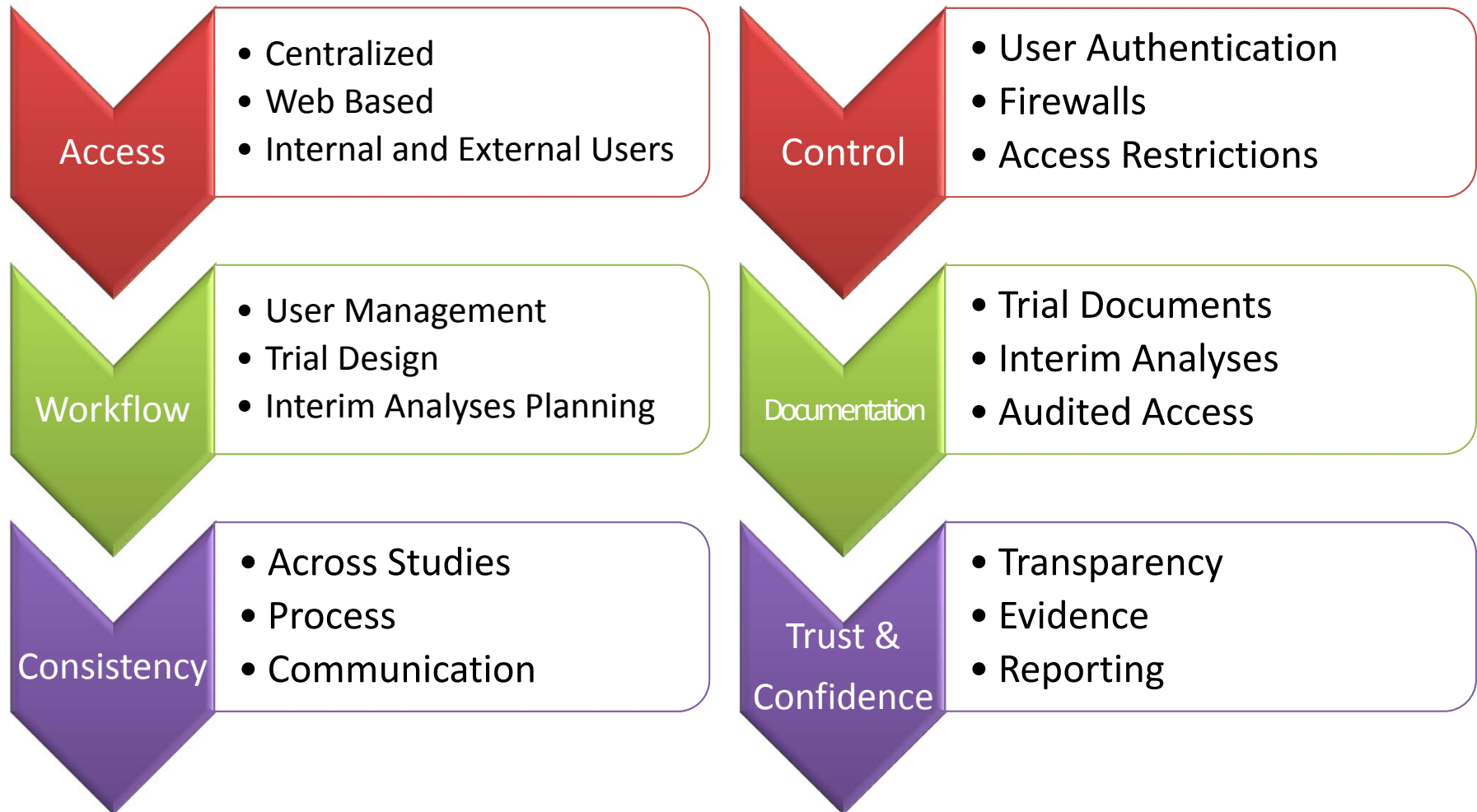
ACES Process



ACES Demo



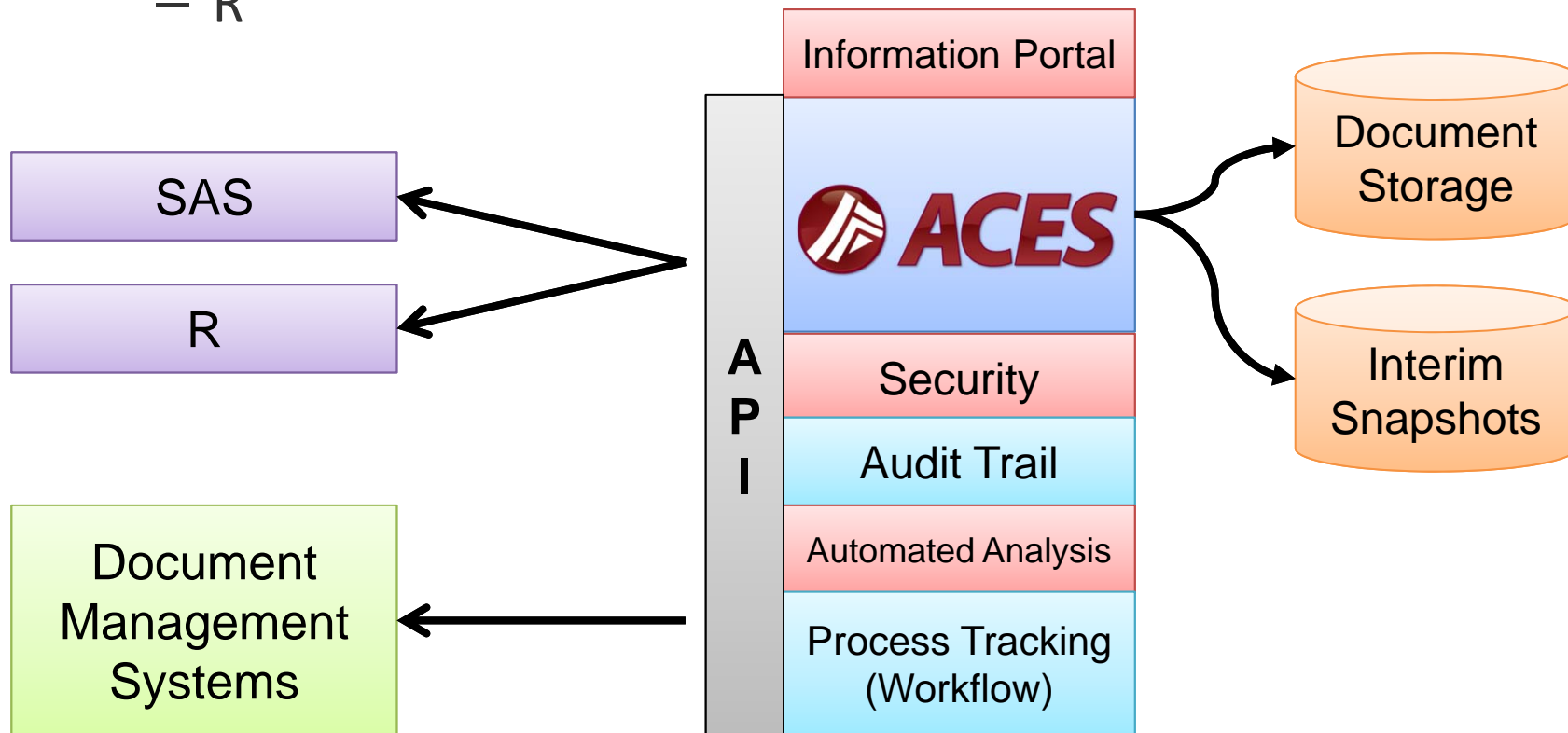
Benefits of Using ACES



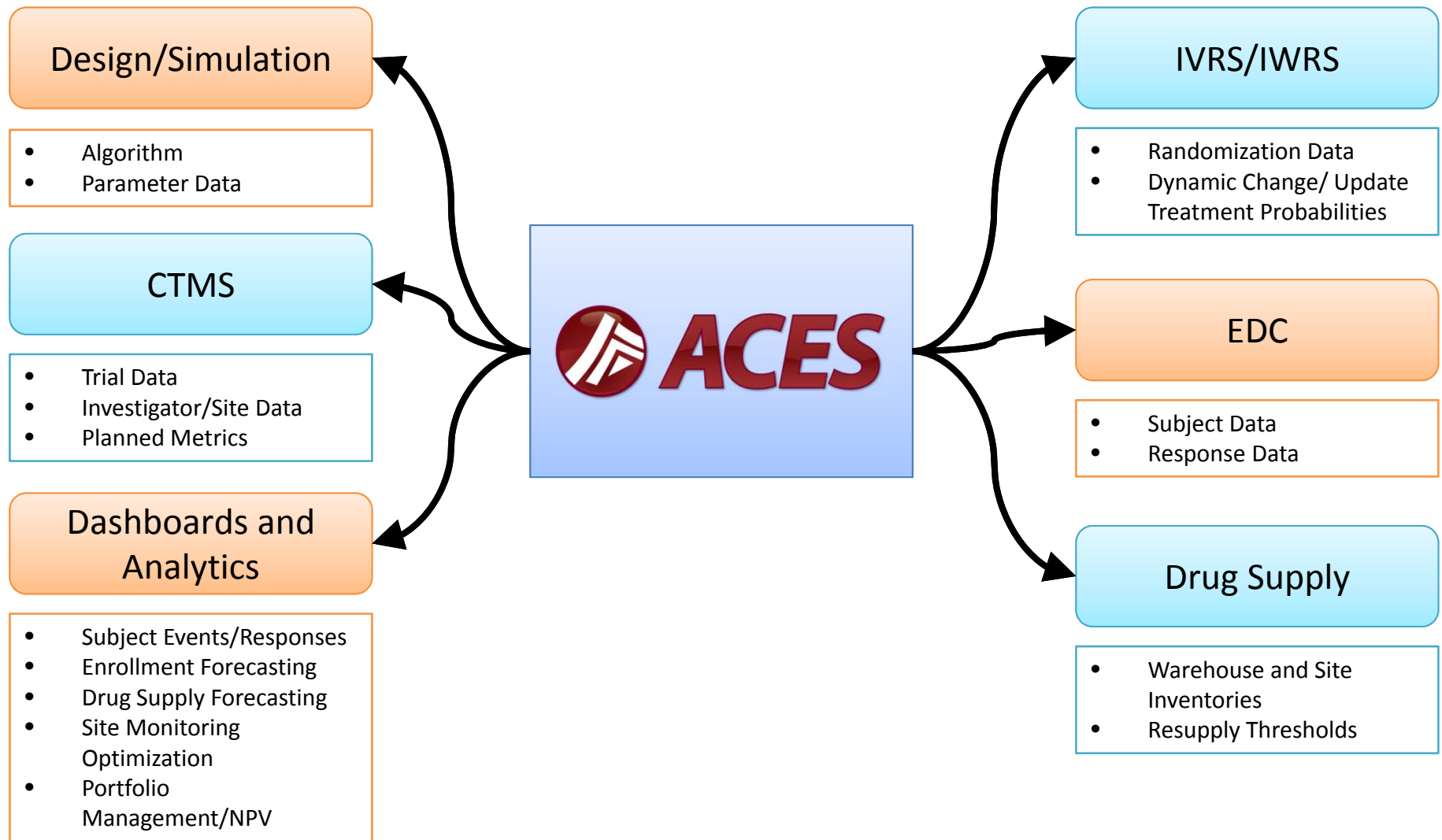
System Integrations

- Statistics Packages
 - SAS
 - R

- Document Management Systems



Future Extensions and Integrations



Actual and Potential Benefits

- Using ACES[®] for executing trials and performing interim analyses enables
 - Isolation of the unblinded trial data to a secure environment
 - Avoids any question of affecting the trial integrity
- All interim analyses process, data, and decisions are captured for a complete trial history
- Guarantees that no changes were made to critical documents after data was unblinded
 - Statistical Analysis Plan (SAP)
 - DMC Charters
 - Protocol Document
- Generates and securely stores blinded or unblinded reports for review by targeted individuals
 - More secure than e-mail or UPS/FedEx
 - Unequivocal assurance that key users (ISC, DMC) have opened documents

Closing Remarks

- **Operational Bias** is greatly reduced by using secure systems, and by limiting access to unblinded data
- **Trial Integrity** is protected by documenting the conduct, logistics, and operation of the trial through security and audit trails
- **Regulatory Confidence** in the consistent execution of adaptive trials by implementing systems that enforce 'best practice' processes

Learn More – Meet Us



[SMi Adaptive Designs in Clinical Development](#)

London, March 26-27, 2012

Eric speaks on protecting trial integrity, reducing operational bias, and building regulatory confidence when conducting interim analyses

[ICSA Applied Statistics Symposium](#)

Boston, June 23-26, 2012

Eric's talk titled, *Optimizing Human Interactions and Information Flow During Interim Analyses*

[ASCO](#), Chicago, June 1-5, 2012

Cyrus Mehta, Cytel President

[BIO](#), Boston, June 19-21, 2012

[DIA](#), Philadelphia, June 24-28, 2012

Exact times & places TBA: [watch cytel.com](http://watch.cytel.com)

Please Take the 5-minute Survey



Please complete the short survey that appears immediately upon webinar end.

Your opinions and interests will help guide our thinking toward shaping an agenda for future webinars.

Thank you.

Learn More - References

- [FDA Draft Guidance on Adaptive Design Clinical Trials](#) (source: www.fda.gov)
- [FDA Guidance on Data Monitoring Committees](#) (source: www.fda.gov)
- [EMA Guideline on Data Monitoring Committees](#) (source www.emea.europa.eu)

Thank You for Joining Today



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