



Recent real-world experiences implementing and supporting several large-scale global clinical trials on OC RDC 4.5.3

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- Introduction-what makes this information timely and vital
- Background of project
- Infrastructure considerations
- Study configuration and Testing
- Data Collection and Discrepancy Management
- Help Desk Observations
- Perspectives from Investigators
- Perspectives from Data Management and Clinical Operations
- Closing Observations and Open Discussion



- **ICON and C3i Experience**

- Global studies
- OC RDC 4.5.3
- Differences between the earlier version, and how these differences impacted:
 - Our work
 - Investigator training
 - Technical site assessments
 - Account creation and management
 - Helpdesk support
 - Query/discrepancy management
- Including some feedback from
 - Investigators
 - Monitors
 - Data Managers
 - Help Desk Support Team



- 3 global studies awarded
 - 1000 sites- including hospitals and outpatient settings
 - Trial to be conducted in at least 40 countries
- Challenges – To use of Oracle Clinical RDC
 - Some, but limited inhouse experience
 - Version available at time of study award 4.5.2
 - Timeline did match the OC release schedule for 4.5.3

- **Management Challenge**

- Determine the benefits of External hosting and implementation or Internal hosting, implementation and systems validation
- Version 4.5.2 deployment and support, On market for sufficient amount of time- known entity, not popular with Investigators.
- Version 4.5.3 near release date. This was the release that was anxiously awaited by many OCRDC users
- ICON needed to determine the best Helpdesk organization to assist with support. Came down to a choice of 2 Life Science helpdesk Organizations



We chose C3i



- **Which Version, 4.5.2 or 4.5.3 / Classic or Onsite.**
- **Hosting, control over the network and data**
- **Network Infrastructure, Resilience of the network, internet circuits, servers, sans firewall. Security on the servers, applications, firewall**
- **Maintenance, Stability of application and Infrastructure: No Downtime!**



Should ICON host the system internally?

- **Considerations**

- **Need to ensure resilience of the network, internet circuits, servers, and firewall.**
- **Security for this large/ multinational project**
- **Internal hosting gives ICON more control over the environment**
- **Internal hosting would be less costly**
- **We could use our newly built, state of the art Data Centre in our Dublin facility**



- **Challenges**

- Building the infrastructure to support round the clock 24/7 use of system
- Determining and meeting support requirements for 24/7 needs
- Building RDC environment around resilience, and eliminating any single points of failure

- **What We Learned**

- Internal hosting does allow more control
- Beware of intruders trying to hack into your systems- pay very close attention to security
- Always have a Plan B- for almost everything!
- If you have the facilities-make use of them- the New Data Centre in Dublin



How do we ensure the best resilience as we build the system?

- **Considerations**
 - **Network and internet circuits**
 - **Firewalls**
 - **Database**
 - **Application servers**
 - **Use of new facility**
 - **Need for replication to data centre in another location- North Wales, PA**



- **Challenges**

- Building an infrastructure to support 24/7
- Metadata servers- New technology for OC RDC
- What happens if Dublin Data Centre crashes
- Building support requirements around the clock
- Building RDC environment for resilience and eliminating single points of failure

- **What we Learned**

- Have a site failover option
- Challenge the system and security



How can we make the system most secure?

- Considerations

- How secure was the external access into ICON?
- Can we audit and report on all attempted intrusions?
- An external security audit may reveal things we did not consider
- What differences are there between versions 4.5.2 and 4.5.3 that may confound security?

- What we Learned

- There will be attempts to hack system
- Audit all attempts at system access
- Lockdown access to servers / database
- Change system passwords on a regular basis
- Have an external auditor perform an audit on a regular basis.



What do we need to do to absolutely minimize downtime and optimize performance?

- Minimum Downtime is the ultimate goal
- Failover to alternate site- PA
- Building RDC environment around resilience, and eliminating single points of failure

• What we Learned

- Have a failover site
- Have a qualified test environment where all changes can be tested prior to production
- Have a robust alerting mechanism in case of emergencies
- Monitor all critical services/points of failure

What version should be validated? Should upgraded version be fully validated?

- Full Systems Validation Completed on v4.5.2 using Internally developed SDLC
- Full Performance Qualification test execution using scripts from an external vendor re-written to ICON SDLC standards
- Test Script execution took 14 Days
- Full Validation completed in 12 weeks
- Decision made to re-run full validation suite for v4.5.3
- Full Validation Complete in 6 weeks, based on lessons learned with 452 validation



- **What we Learned**

- If you have the resources it can be done.
- User Requirements for v4.5.2 and v4.5.3 almost same, so documents were almost cut and paste
- Test scripts needed to be changed due to new User Interface
- Test Script execution complete in 4 days
- Write test scripts so they can be re-used for regression testing.

Thoughts on 453 ?

- **Have been live for 5 Months**
- **Have applied up to Patch 4.5.3.10**
- **No Unscheduled downtime**
- **Very Very Stable Application, no bugs outstanding!**
- **The end users like it!**





- Considerations

- CRF designs were not completely finalized when work was to begin
- No clear specifications were available for protocol required pages
- Some legacy approaches within client DM rules had to be reconsidered
- Neither client nor ICON knew all the changes expected with upgrade to 4.5.3
- Timelines shifted during the configuration period. Meeting client expectations with a quality database was always our first goal
- Once database was built in 4.5.2, migrating to 4.5.3 needed to be as simple as possible
- Clinical teams have a greater roll in system testing within the electronic environment

- What we Did

- Work began on most up to date CRF design, which was not the first trial to start
- Client and ICON agreed with protocol specific page designs
- Keeping the team motivated during upgrade period added to success
- Training materials were revised once the upgrade was completed



- **What we Learned**

- Time is best used without adding the challenge of upgrading and migrations during study configuration
- Testing will be a major function for future trials, and our clinical teams will continue to improve in participation
- Client training for upgraded version was pivotal prior to participation in system testing
- Data Management needs insight into site progress with system access and data entry



- **Considerations**

- With an END POINT trial plan, multiple triggers are necessary for proper notification when events occur
- Within the program 3 different studies required 3 separate data collection plans
- Different groups require access to specific CRF details
- The integration of IVR data into the EDC would benefit the management of sites, and allow for overview of data entry progress within a single system



- **How we Managed this**

- One platform was developed and then amended to meet each separate study needs
- First study which went live served as “springboard” for other studies- reducing timelines for “live system”
- Clinical and Data teams can easily work within system on any/or all studies within this program
- Time did not allow for full integration, so two separate reporting tools are compared to define site activity versus data entry



- **What we Learned**

- Early agreement on system integration functional specifications is critical
- Maximize team members within similar trial environments wherever possible
- The ability to integrate data reduces the complexities of site management and data collection, and should be used wherever possible





C3i and ICON - full partnership in site support and system management in OC RDC

- Considerations

- Bring multiple cultures together and begin site support for large global trial
- Deliver seamless service to client and sites
- Keep communication channels open as changes occur
- Prepare for rapid start of patient data entry
- Ensure that training is planned to meet needs of all stakeholders

What we Did



- C3i took immediate responsibility for site management in EDC
 - Led the Site Assessment process
 - Developed reporting tools for submission to clinical teams and clients
 - Maintained list of needed items and updated weekly
 - Developed re-usable PI and Site training programs
 - Took full responsibility for site access to system

What we Did



- **ICON maintained responsibility for Clinical teams**
 - Follow up on items for C3i to ensure site access
 - Training provided to ICON teams with C3i colleagues as participants
 - PI and Site access or training follow-up managed by clinical teams



What we learned about 4.5.3 vs. Earlier Versions

- Site Assessment process for 4.5.3 was much less cumbersome for investigator site personnel
- Less help desk call volume during startup (in & out)
 - No need to install plug-in
 - No need to install Citrix
 - No need to deal with investigator staff lacking Administrator rights on their PC
- Reduced need to provision laptops to sites
- Training is still very critical
 - For site satisfaction
 - For keeping help desk call volume low after study startup

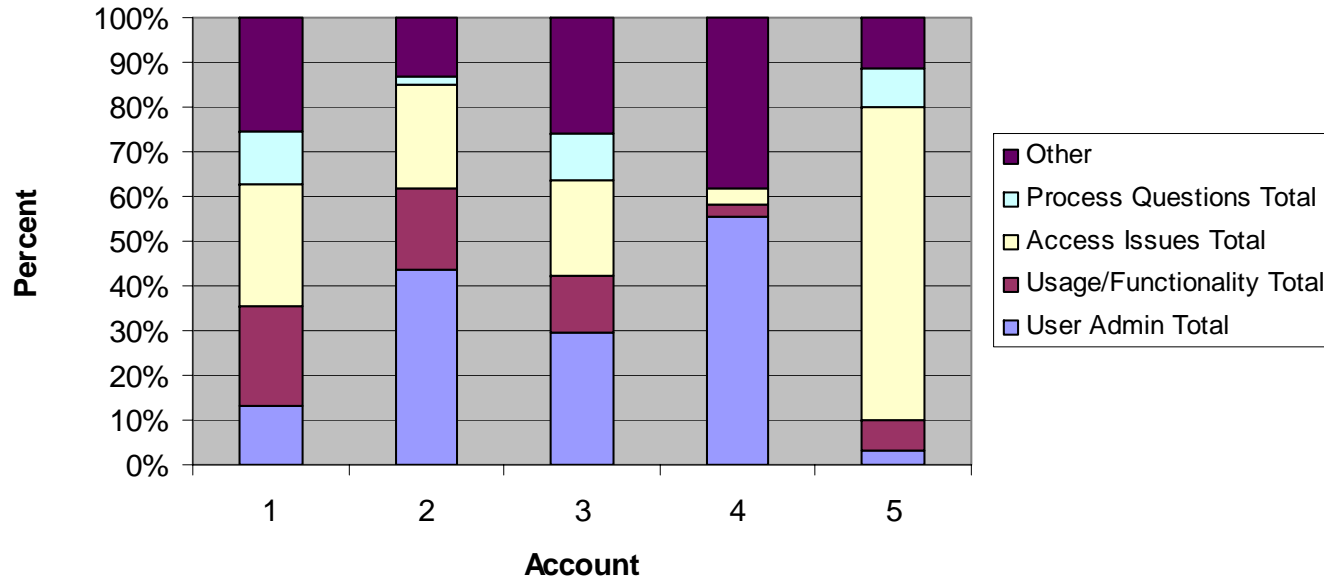
Help Desk Perspective (cont)



NOTE: Source of this data is from [multiple C3i clients who use OC-RDC.](#)

| | |
|--------|-------|
| Acct 1 | 4.5.1 |
| Acct 2 | 4.5.1 |
| Acct 3 | 4.5.3 |
| Acct 4 | 4.5.3 |
| Acct 5 | 4.5.3 |

% of Incidents (June - Aug)

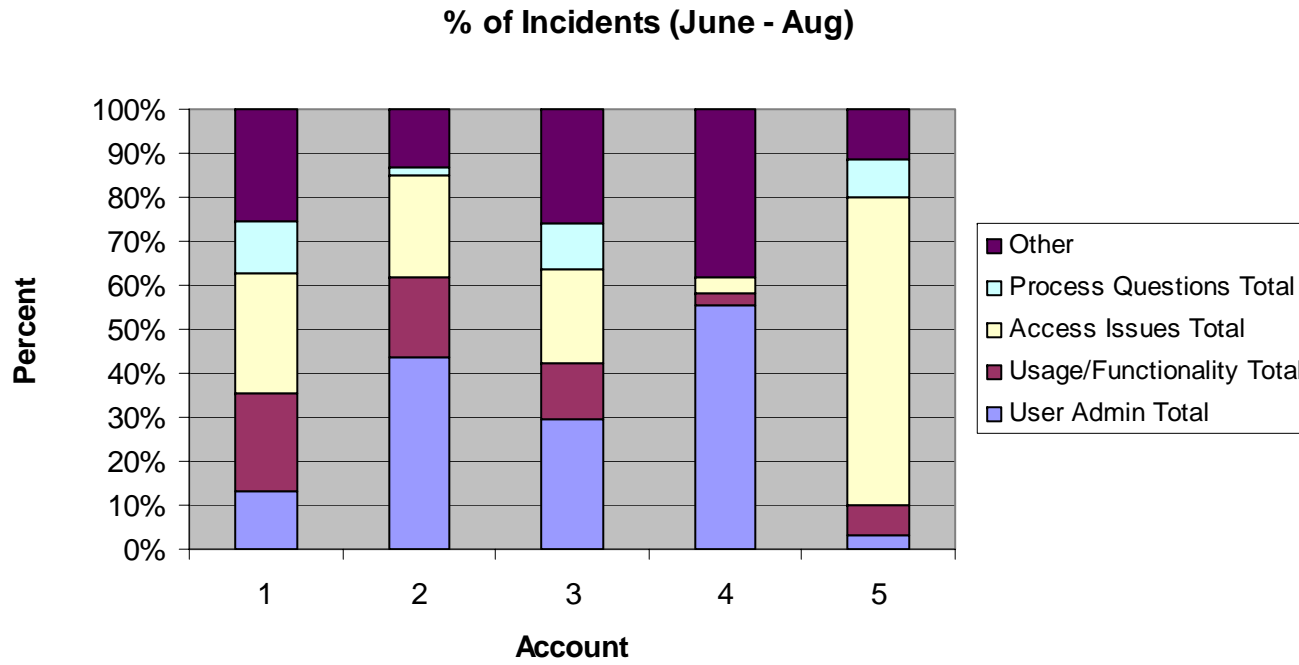


Observation 1

There are 2 client accounts with unique attributes worth mentioning

- Account 4 is still in startup so case mix is very different than others
- Account 5 is relatively small compared to others, so % mix fluctuates more than others

Help Desk Perspective (cont)



NOTE: Source of this data is from multiple C3i clients who use OC-RDC (not just ICON).

| | |
|--------|-------|
| Acct 1 | 4.5.1 |
| Acct 2 | 4.5.1 |
| Acct 3 | 4.5.3 |
| Acct 4 | 4.5.3 |
| Acct 5 | 4.5.3 |

Observation 2

% of incidents about "Usage/Functionality" appears to be somewhat lower for accounts using version 4.5.3

- Accounts 3 & 5 (V 4.5.3) → approximately 12% and 7% respectively
- Accounts 1 & 2 (V 4.5.1) → approximately 22% and 18% respectively

- Note: Can't really compare Account 4 for this analysis since bulk of sites are still in startup phase.



Considerations

- For a clinical team, with multiple ongoing functions, each additional group who contributes adds to trial complexity
- Keeping all parties updated and moving toward the same goal can prove challenging
- The rate at which countries are ready for patient enrollment within a clinical trial varies greatly
- Sites expect timely responses when questions or problems arise
- One time training for any system is most preferred by sites
- Time spent in retraining for upgrades may be viewed as 'wasted time'



- What we Did

- In anticipation of upgrade to 4.5.3, we only trained sites and clinical monitors who were likely to need access to the earlier version
- We managed site access planning at a country level, by providing timeline estimates for each country
- Site training in 4.5.3 was in multiple parts including online training, on-site training and a written reference manual

Other Perspectives

Investigators and Clinical Teams



- On line training with the option of repeating any training at any time allows sites to perform better during data entry
- The training plans and deployment for the sites and clinical teams proved very beneficial to the trial



- **What We Learned**

- Clear expectations for all reports, meetings and interactions must be stated
- It is important for all parties to understand the requirements per country for site participation. This helps manage expectations and timelines
- Frequent review of helpdesk call logs can define trends and training opportunities
- “Just in time” training seems to work best for any EDC system, as use of system is the only mechanism that reinforces learning
- 4.5.3 proved to have many intuitive and enhanced functions which made the re-training experience very positive for those sites and monitors who began work in the earlier version

- Based upon years of experience in Oracle Clinical environment, the biggest challenges involved upgrading and managing the timelines for taking all three trials live.
- Clinical teams have a greater roll in system testing within the electronic environment





- Discussion

- Follow-up Questions

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- Thank you!