

Architecture Design of Integrated Information Management System for Clinical Trials

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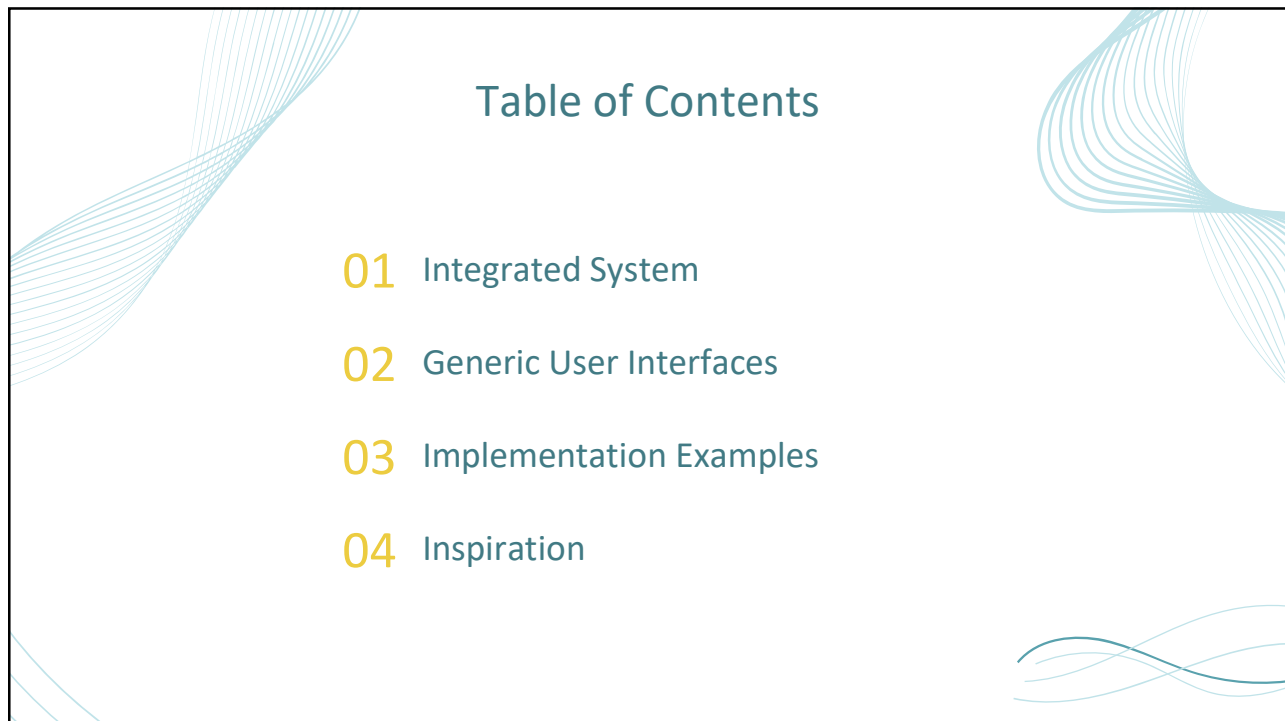


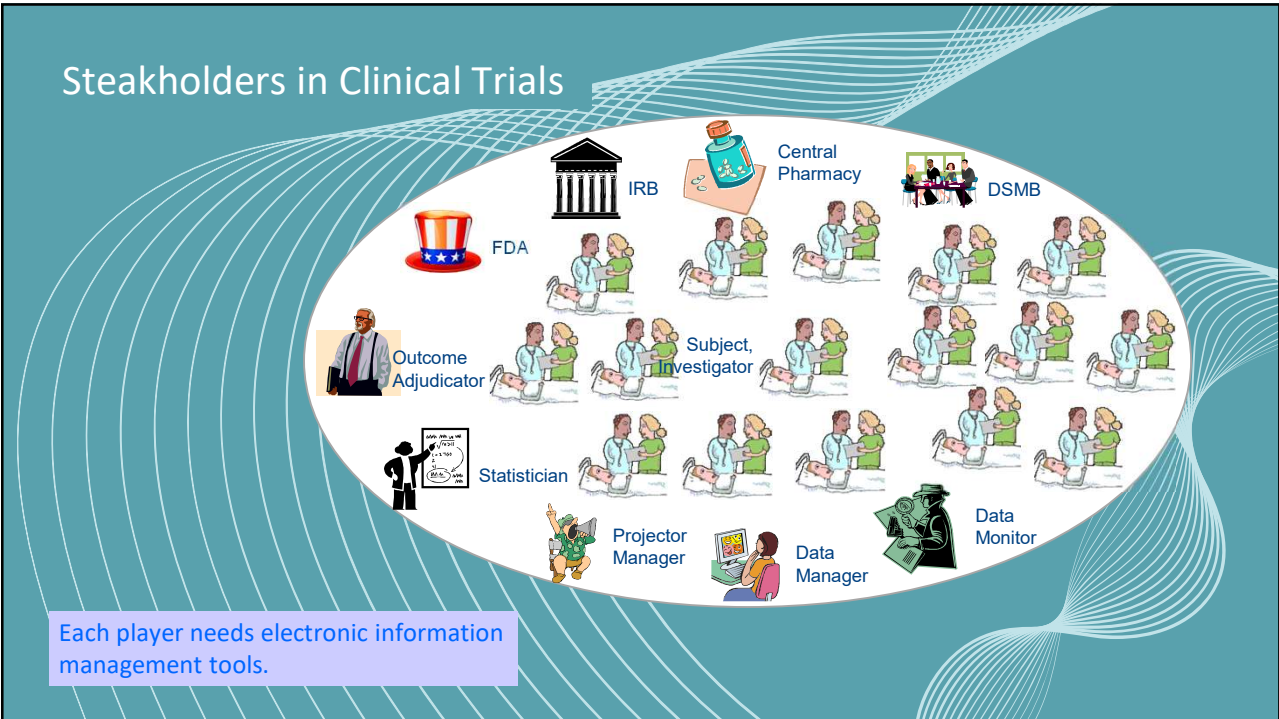
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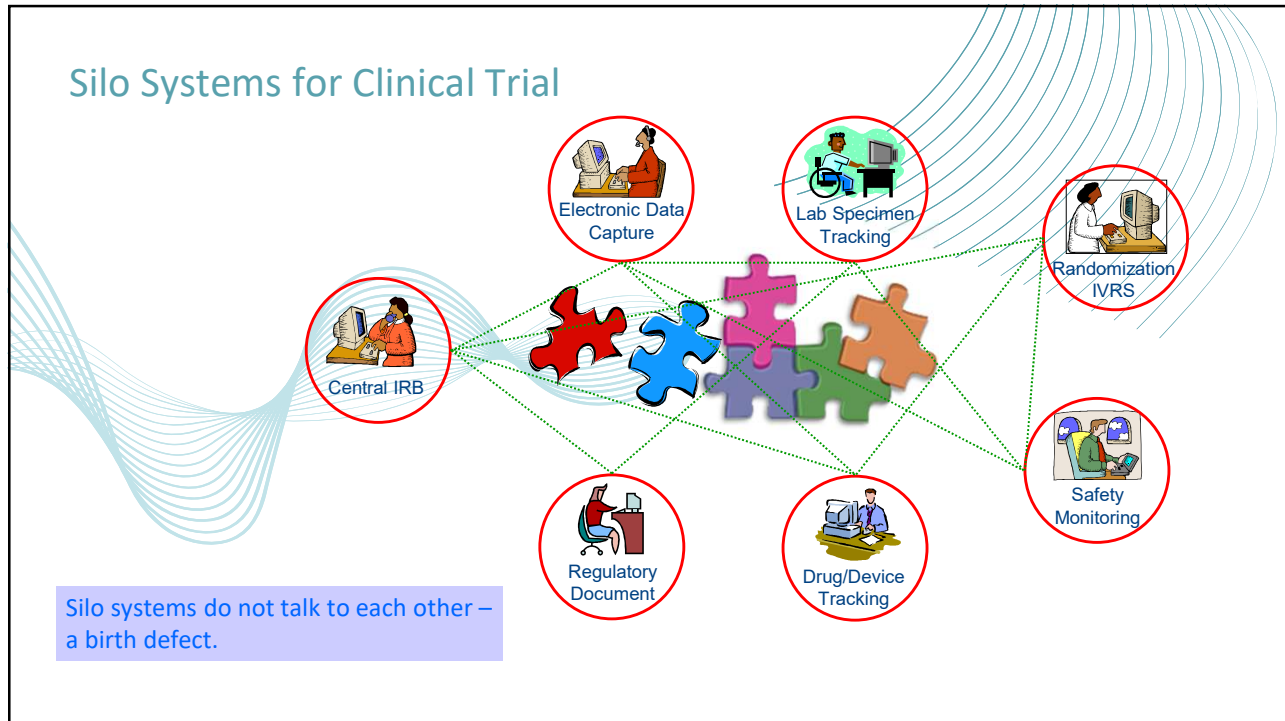
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01 Integrated System

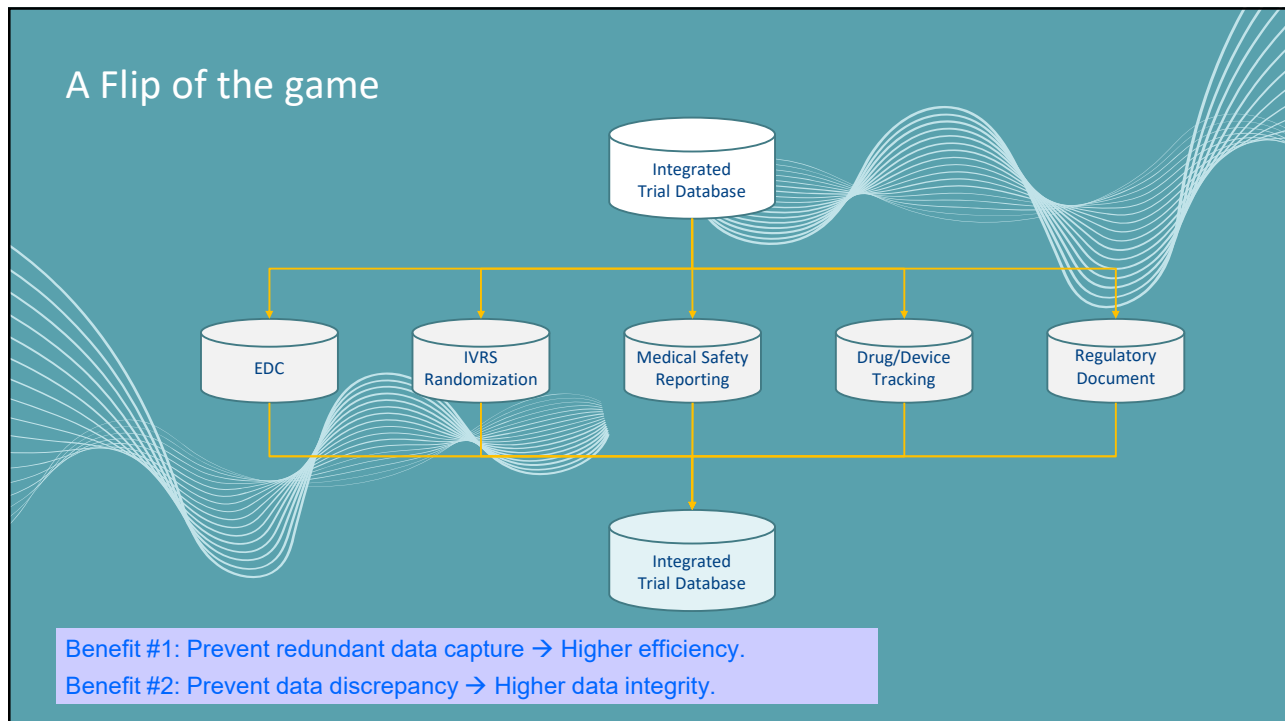
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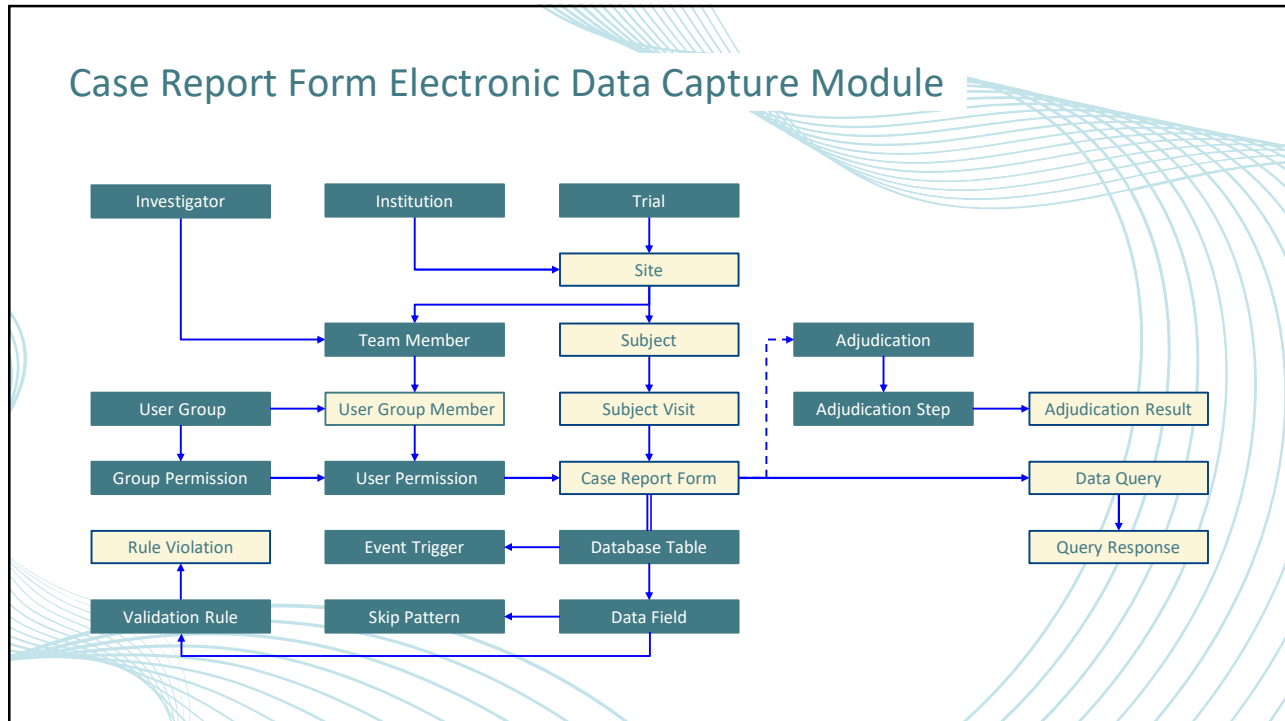
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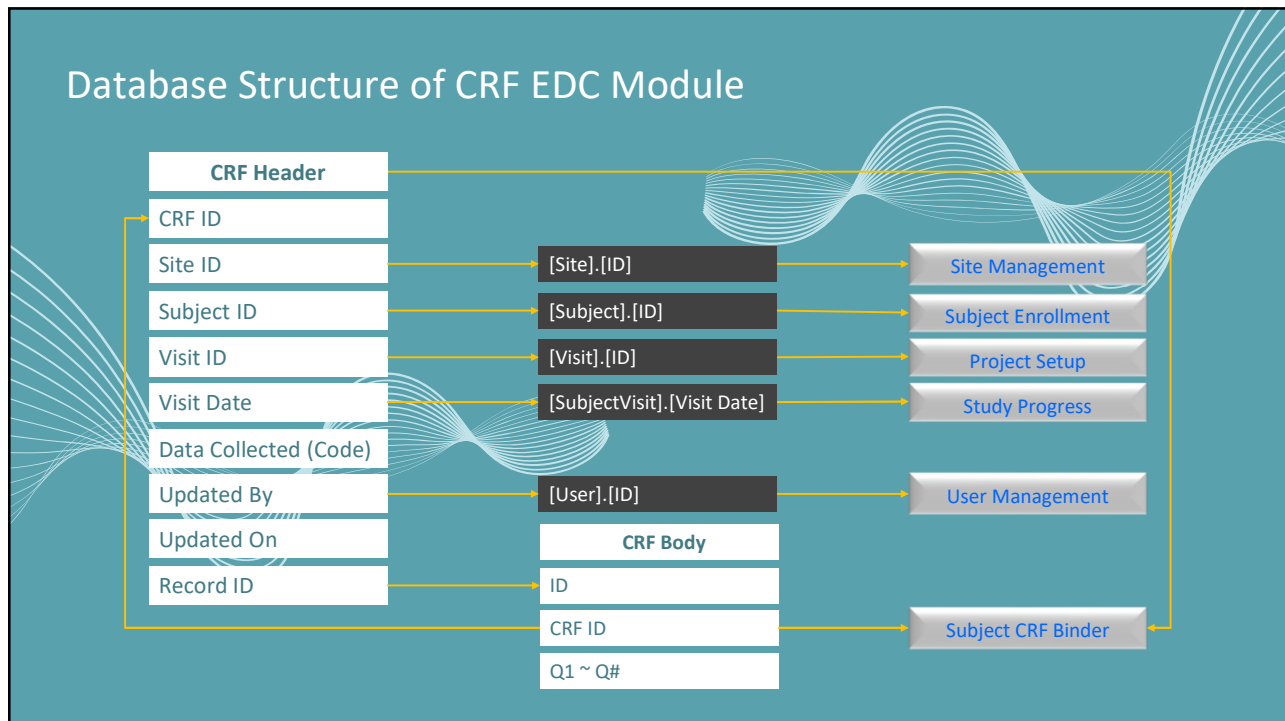
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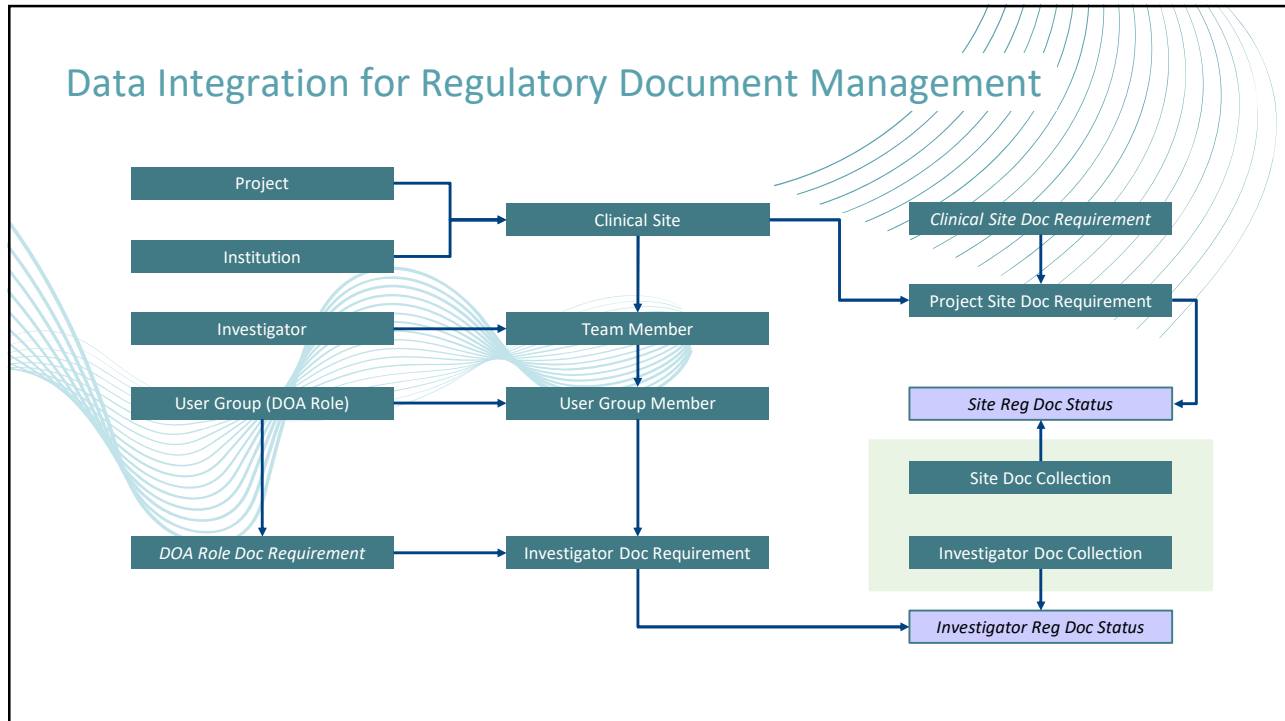
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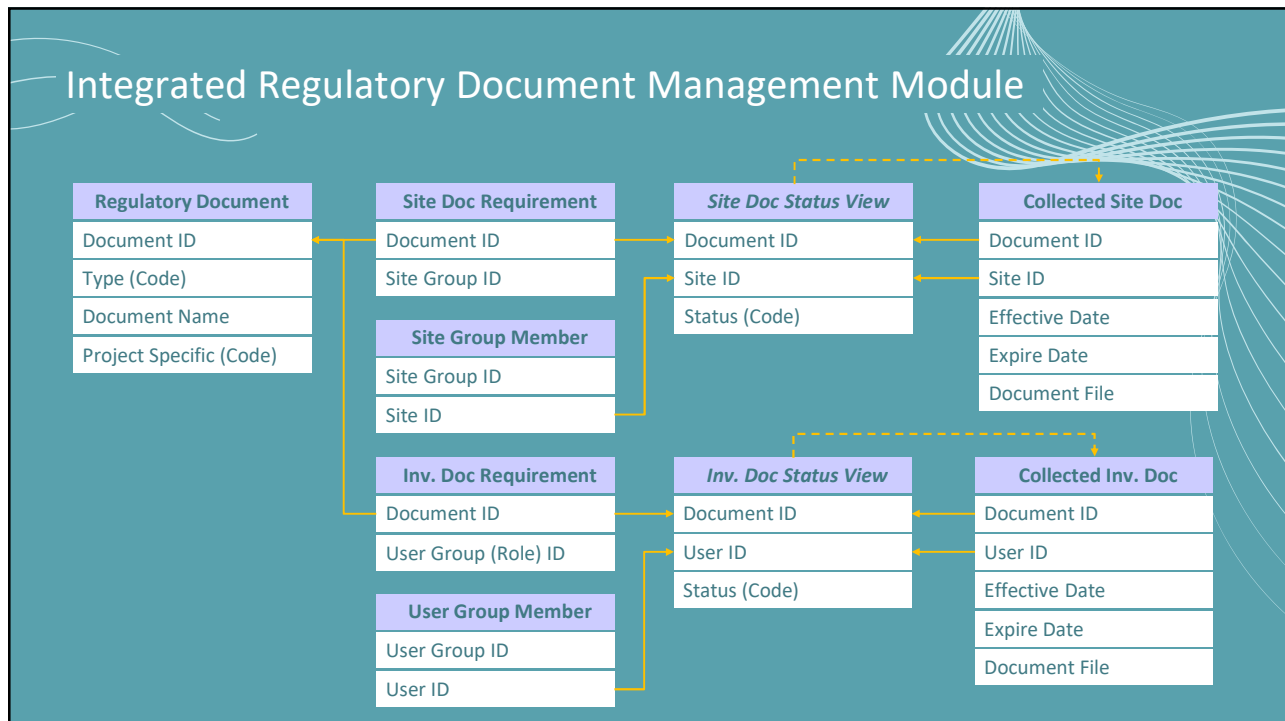
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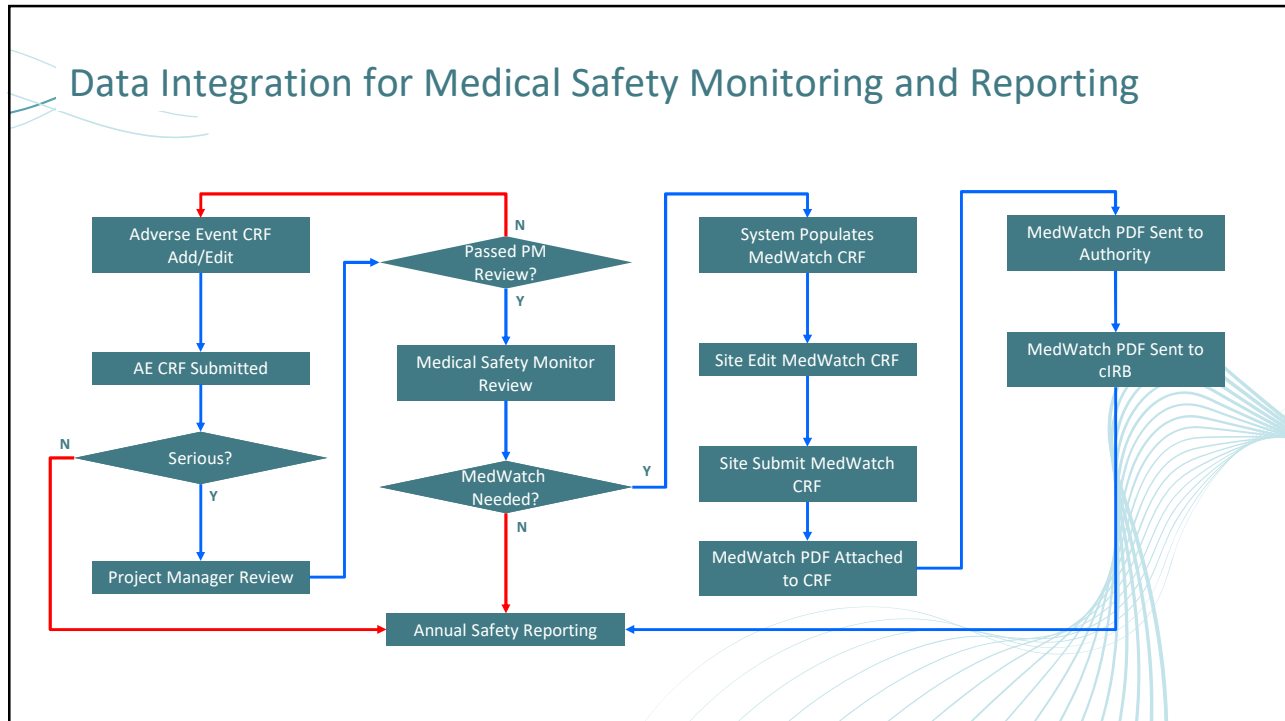
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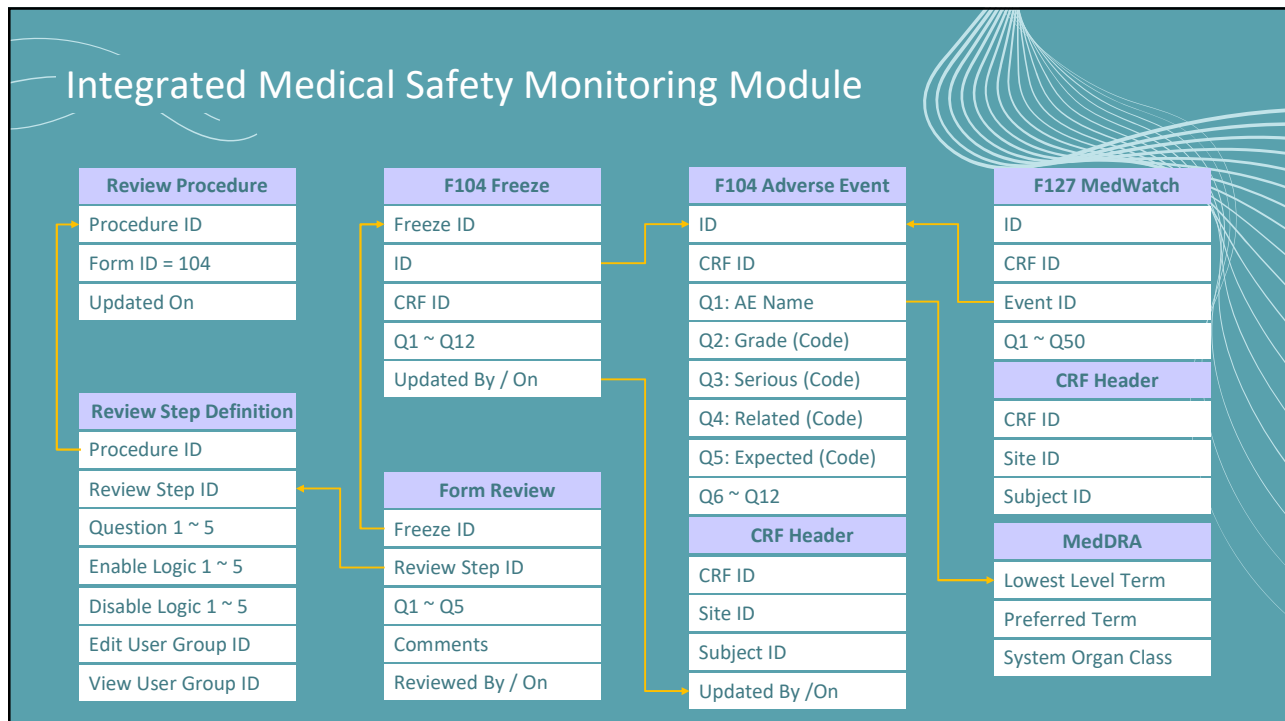
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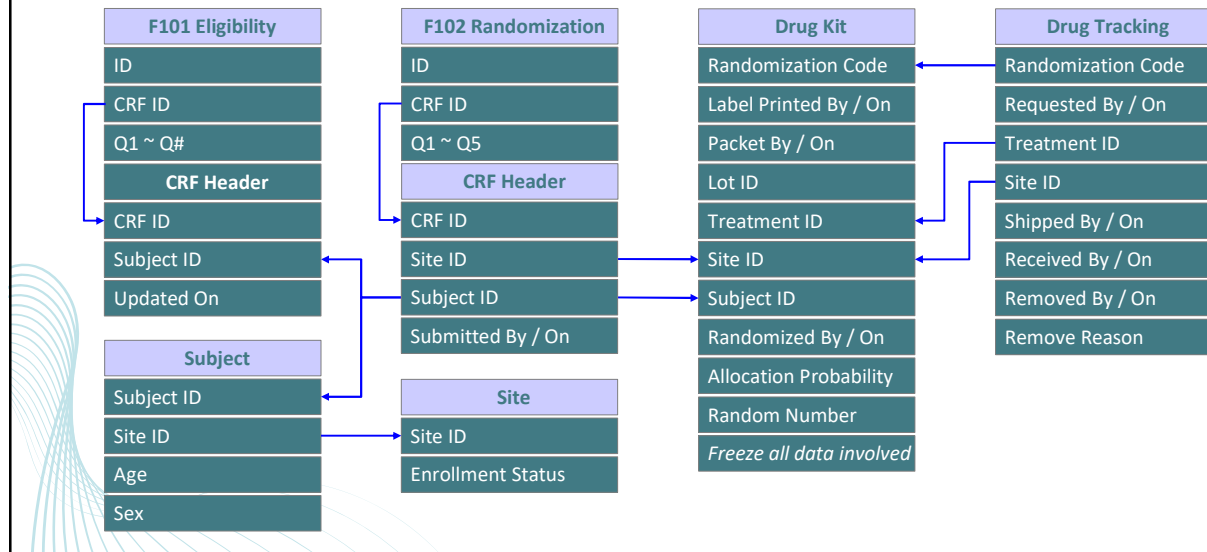


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Integrated Randomization & Trial Supply Management Modules



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02

Generic Building Blocks

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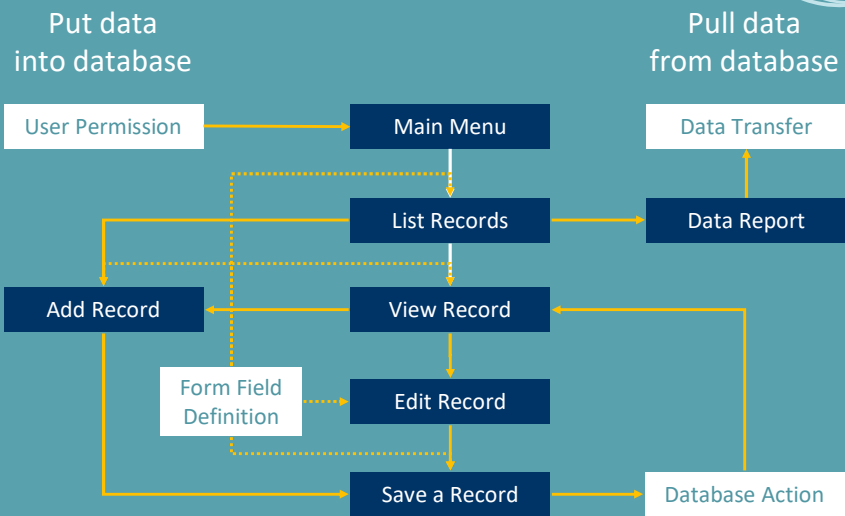
The Great Innovation of Container



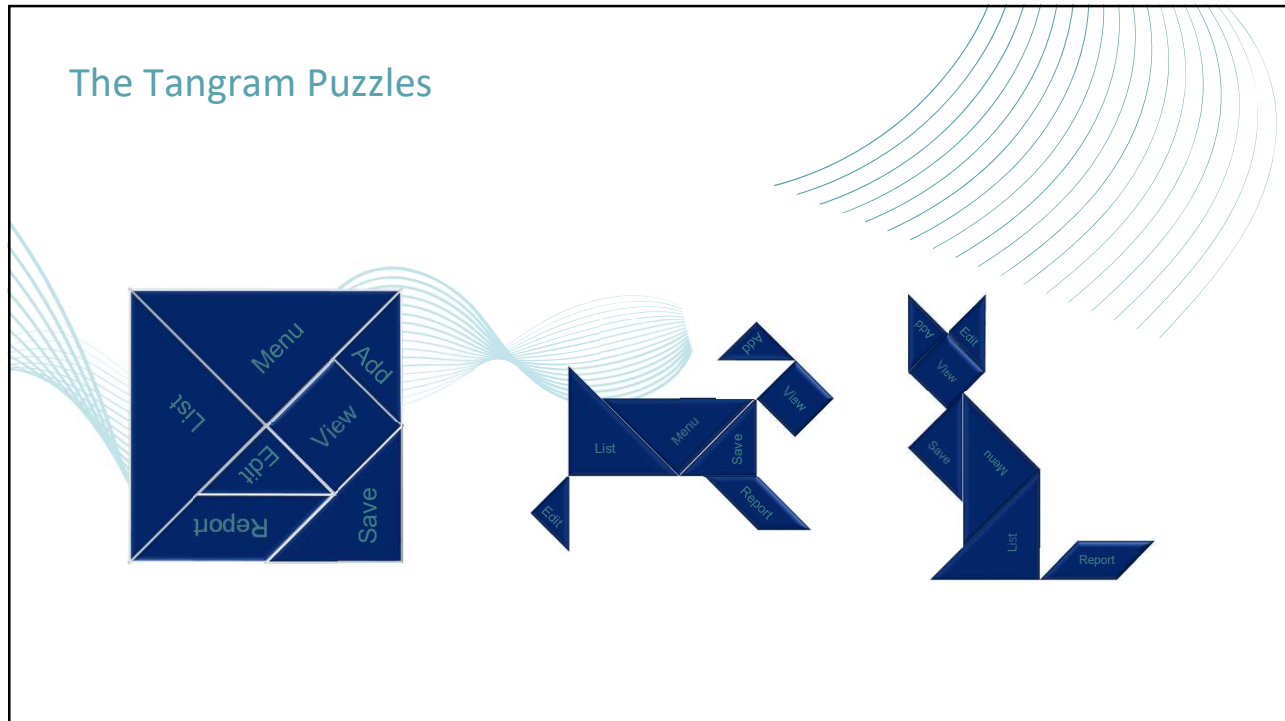
Different contents, same shape of containers.

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Management Information System Basic Function Analysis



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Generic [List Records] Page

1. [List Records with Form ID](#)
2. [List only Fields with 'For List = Yes'](#)
3. [Record sort by selected field data value](#)
4. [Record filter by specific value in selected field](#)
5. [Page navigation \(First, Next, Previous, Last\)](#)
6. [Change page size](#)
7. [Link to \[View Record\] page for individual record](#)
8. [Generic basic summary function](#)
9. [Show \[Add Record\] button for authorized users](#)

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Generic [View a Record] Page

1. View a Records from a Table with the Form ID and Record ID specified
2. Display question number, name, (options), response
3. For CRFs, display CRF Header Information:
 - Site, Subject, Visit
 - Submit Date/Time, Rule Status, DCR Status, Verify Status
4. Show action buttons for authorized users:
 - [Add], [Edit], [Delete], [View Audit], [List Records],
 - [Verify], [Accept], [DCR] [Lock], [Unlock]
5. Display rule violation flags and responses to rule violation
6. Display data clarification requests and corresponding responses

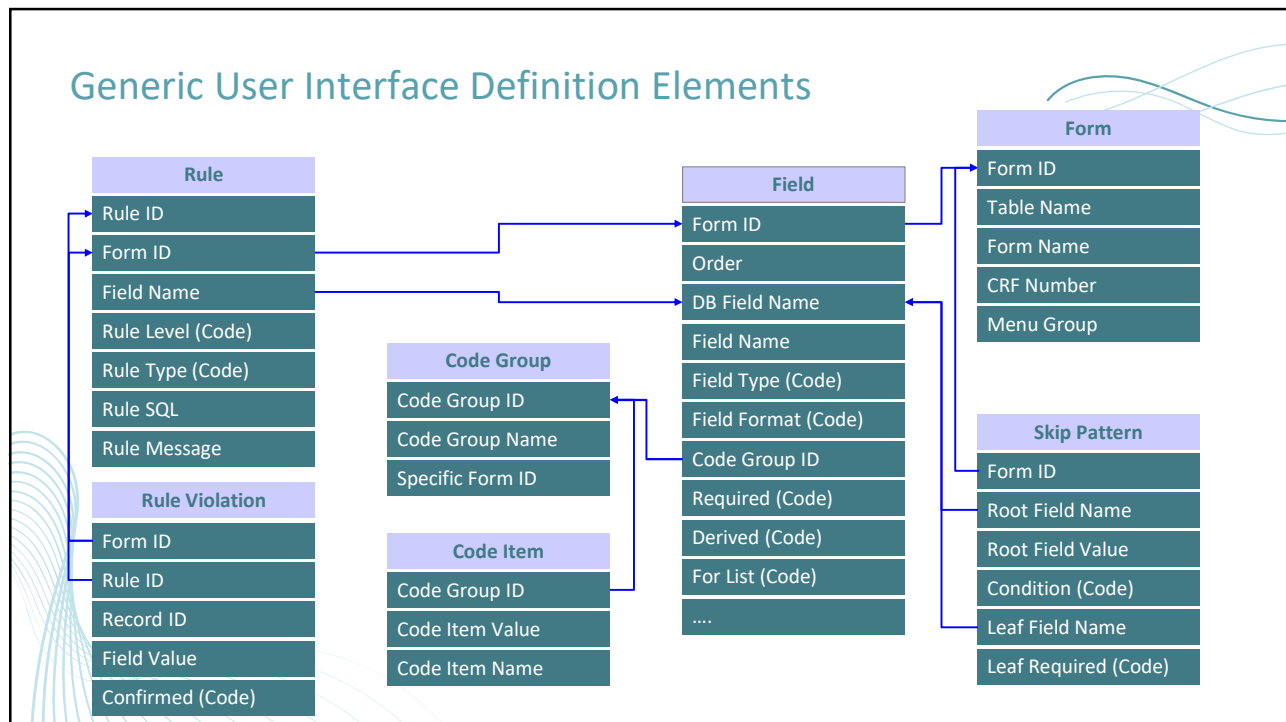
Source: www.clinicaltrials.gov searched on 03/04/2022

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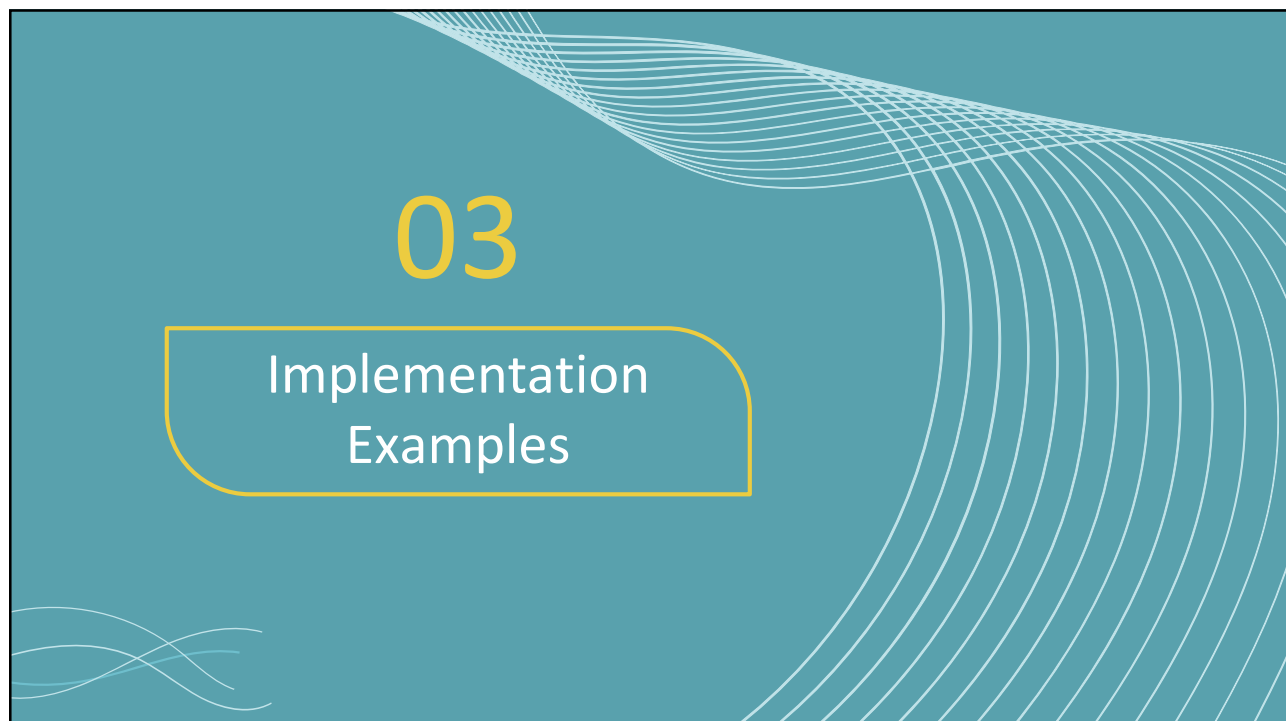
Generic [Edit a Record] Page

1. Edit a record specified by Form ID and Record ID
2. Add a new Record when Record ID = 0
3. Display question number, name, description
4. Provide data entry fields based on field types with previous data displayed
5. Provide response options condition to response values in other fields
6. Enforce skip pattern logic
7. Flag fields required for record saving
8. Add required [Reason for Change] for editing record
9. Show [Save], [Cancel] buttons

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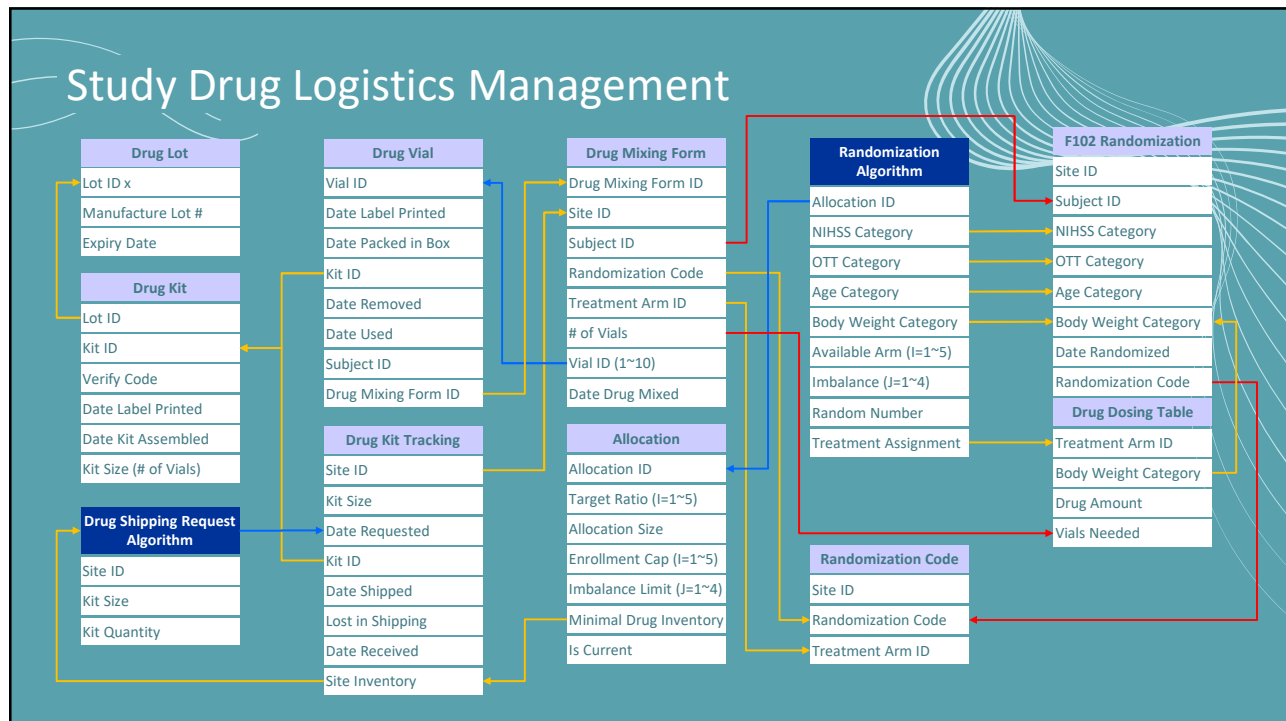
STRATEGY FOR IMPROVING STROKE TREATMENT RESPONSE (SISTER) TRIAL



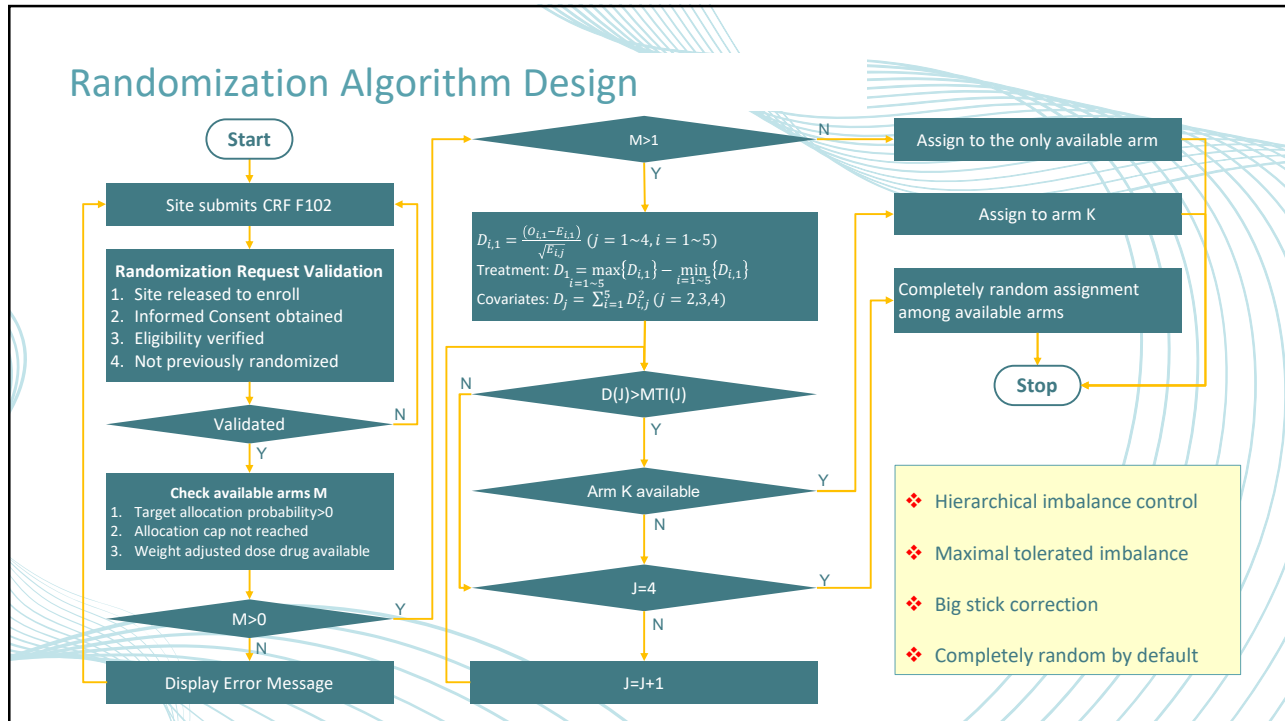
ClinicalTrials.gov registration ID: [NCT05948566](https://clinicaltrials.gov/ct2/show/study/NCT05948566)

1. Dose escalation from 3mg/kg to 5, 7, and 10 mg/kg for the first 50 subjects
2. Response adaptive allocation ratio updated for every 50 following subjects
3. Body weight adjusted infusing drug amount for each dose level
4. Site investigators and subjects are fully blinded
5. Site pharmacists are unblinded and responsible for infusing bag mixing
6. Minimize study drug water due to expiration
7. Control treatment imbalances
8. Control baseline NIHSS, Onset To Treat time, age imbalance
9. Protect allocation randomness

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Treatment Imbalance Assessment

		Arm 1	Arm 2	Arm 3	Arm 4	Arm 5	Total
Target Allocation		1	$\sqrt{1.3}$	$\sqrt{1.5}$	$\sqrt{1.7}$	$\sqrt{2}$	
Target Allocation Probability	P_i	0.164	0.187	0.201	0.214	0.232	1
Observed	O_i	9	8	4	10	7	38
Expected	E_i	6.247	7.123	7.651	8.145	8.835	38
Imbalance	D_i	2.753	0.877	-3.651	1.855	-1.835	0

Option #	Assessment method	Formula	Result
1	Imbalance range	$\max_{i=1-5} \{O_i - E_i\} - \min_{i=1-5} \{O_i - E_i\}$	6.404
2	Scaled range	$\max_{i=1-5} \left\{ \frac{O_i - E_i}{\sqrt{E_i}} \right\} - \min_{i=1-5} \left\{ \frac{O_i - E_i}{\sqrt{E_i}} \right\}$	2.421
3	Euclidean distance	$\sqrt{\sum_{i=1}^5 (O_i - E_i)^2}$	5.337
4	Pearson's Chi-square test	$\sum_{i=1}^5 \frac{(O_i - E_i)^2}{E_i}$	3.867 P-value=0.4243
5	Likelihood ratio test	$-2 \sum_{i=1}^5 O_i \ln \left(\frac{E_i}{O_i} \right)$	4.088 P-value=0.3943

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Baseline Covariate Imbalance Assessment

	Observed						Total	Expected					Imbalance $(O_{ji} - E_{ji})/\sqrt{E_{ji}}$				
	Arm 1	Arm 2	Arm 3	Arm 4	Arm 5	Arm 1		Arm 2	Arm 3	Arm 4	Arm 5	Arm 1	Arm 2	Arm 3	Arm 4	Arm 5	
Category 1	5	6	0	1	1	13	4.73	4.73	0.59	0.59	2.36	0.13	0.59	-0.77	0.53	-0.89	
Category 2	3	2	1	0	3	9	3.27	3.27	0.41	0.41	1.64	-0.15	-0.70	0.92	-0.64	1.07	
Entire Study	8	8	1	1	4	22	8	8	1	1	4						

$$\chi^2 = \sum_{j=1}^2 \sum_{i=1}^5 \frac{(O_{ji} - E_{ji})^2}{E_{ji}} = 4.936 > \chi_{4,0.7}^2 = 4.878$$

If the subject has in category 1 and arm 5 is available, vote for Arm 5.
 If the subject has in category 2 and arm 2 is available, vote for Arm 2.
 Otherwise, skip this covariate.

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Pediatric Influence of Cooling duration on Efficacy in Cardiac Arrest Patients (P-ICECAP)



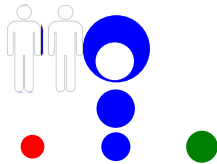
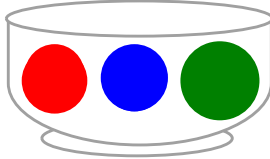
ClinicalTrials.gov registration ID: [NCT05376267](https://clinicaltrials.gov/ct2/show/study/NCT05376267)

1. Emergency treatment require immediate randomization
2. Plan to enroll up to 900 subjects from about 45 sites in US
3. No study drug involved
4. No baseline covariate balancing required
5. Burn-in period with three-arm equal allocation for the first 150 subjects
6. Response adaptive allocation among 10 arms updated every 10 weeks
7. Enrollment history: 18±6 subjects per 10 weeks for the first 145 subjects
8. Wish to control treatment imbalance

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Mass-Weighted Urn Design

Target allocation = Desired allocation = $1 : \sqrt{2} : \sqrt{3} = 0.2412 : 0.3411 : 0.4177$



Start the with one ball for each arm. Mass of each ball is proportional to the target allocation ratio, in continuous format.

Total mass in the urn = α units, a pre-specified value.

Randomly draw a ball with probability proportional to the mass of each ball.

Assign the subject accordingly.

The mass of the ball is reduced by 1 unit.

This 1 unit mass is re-distributed to each arm based on the target allocation.

Repeat steps 3 to 5 until the end of the study.

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Simulation Results

10-arm equal allocation after 20 subjects, 50,000 simulation runs						
Number of empty arms	Complete Random	Mass-weighted Urn Design				
		$\alpha = 4$	$\alpha = 6$	$\alpha = 8$	$\alpha = 10$	$\alpha = 12$
≥ 1	78.50%	0.5%	3.23%	7.77%	14.16%	19.54%
≥ 2	34.76%	0	0	0.08%	0.29%	0.38%
≥ 3	7.33%	0	0	0	0	0
≥ 4	0.71%	0	0	0	0	0

10-arm unequal allocation (1 : 1.1 : 1.2 : 1.5 : 1.7 : 1.8 : 1.9 : 2 : 2.5 : 3) after 20 subjects, 2,380 simulation runs						
Number of empty arms	Complete Random	Mass-weighted Urn Design				
		$\alpha = 4$	$\alpha = 6$	$\alpha = 8$	$\alpha = 10$	$\alpha = 12$
≥ 1	86.38%	6.51%	12.14%	19.75%	29.96%	37.35%
≥ 2	48.48%	0	0.55%	0.76%	1.55%	4.41%
≥ 3	14.90%	0	0	0	0.04%	0.08%
≥ 4	2.18%	0	0	0	0	0
Imbalance in Euclidian Distance	2.71±1.27	1.41±0.45	1.55±0.52	1.67±0.58	1.78±0.63	1.87±0.68

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Unconditional Allocation Probability

Mass-weighted Urn Design										
10-arm unequal allocation (1 : 1.1 : 1.2 : 1.5 : 1.7 : 1.8 : 1.9 : 2 : 2.5 : 3) after 20 subjects, 2,380 simulation runs										
Sequence Order	Arm 1	Arm 2	Arm 3	Arm 4	Arm 5	Arm 6	Arm 7	Arm 8	Arm 9	Arm 10
1	0.0565	0.0621	0.0678	0.0847	0.0960	0.1017	0.1073	0.1130	0.1412	0.1695
2	0.0603	0.0653	0.0706	0.0868	0.0982	0.1028	0.1069	0.1122	0.1360	0.1611
3	0.0637	0.0684	0.0726	0.0885	0.0974	0.1011	0.1050	0.1092	0.1329	0.1612
4	0.0665	0.0703	0.0737	0.0887	0.0966	0.0987	0.1014	0.1049	0.1354	0.1638
5	0.0689	0.0715	0.0732	0.0871	0.0937	0.0953	0.0996	0.1057	0.1385	0.1666
6	0.0686	0.0709	0.0719	0.0838	0.0919	0.0972	0.1005	0.1072	0.1418	0.1663
7	0.0679	0.0691	0.0681	0.0796	0.0937	0.1002	0.1032	0.1109	0.1433	0.1640
8	0.0655	0.0649	0.0649	0.0807	0.0954	0.1023	0.1057	0.1147	0.1425	0.1635
9	0.0625	0.0619	0.0595	0.0824	0.0986	0.1050	0.1083	0.1179	0.1369	0.1669
10	0.0579	0.0580	0.0548	0.0859	0.1019	0.1074	0.1100	0.1180	0.1364	0.1697
20	0.0630	0.0687	0.0731	0.0788	0.0959	0.1018	0.1078	0.1129	0.1345	0.1635

Unconditional allocation probability shifts toward equal allocation when alpha is small.
Need further research to eliminate or reduce this shit.

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Inspiration

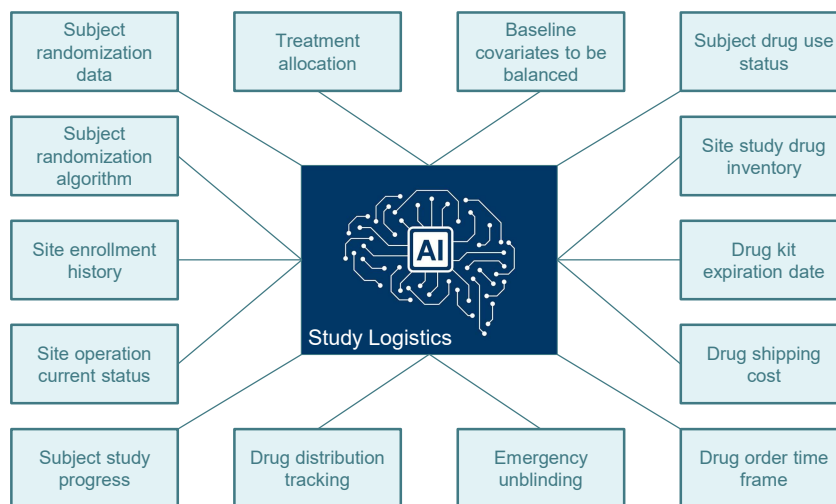
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Conclusions

1. Creation of an integrated information system is feasible
2. Generic building blocks increase system development quality and efficiency
3. Development of complex system requires collaboration from stakeholders

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Opportunity to be a Creative Thinker



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How are We Working?



Work correctly done, automatically!



Work correctly done, always!



Work done, correctly!



Job done, finally.

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Thank you!

Contact me at: zhaow@musc.edu

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