Datahåndtering i praksis

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Oslo universitetssykehus

Hva er hensikten med å utføre datahåndtering i en klinisk studie?

- Det overordnede målet med datahåndtering er å opparbeide en database hvor data er identiske med de innsamlede data slik de foreligger i kildedokumentene
- Databasen skal inneholde data som er identifiserbare, av god kvalitet, lett anvendelige og tilpasset sitt formål
- Databasen som foreligger ved studiens slutt skal inneholde sporbare data.
- Og hva er av god kvalitet? Datakvalitet kan defineres som fravær av feil som har betydning for resultatet av studien.

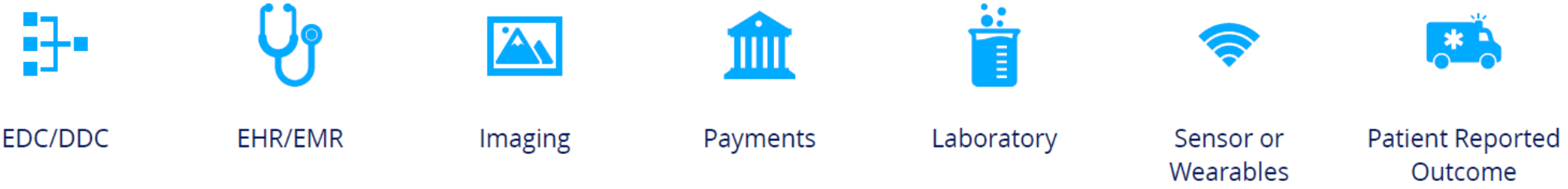
Så hva er studiedata

Studiedata omfatter all informasjon som genereres, samles inn eller brukes i forbindelse med studien, alt fra eksisterende kildedata til studiespesifikke vurderinger.

- Studiedataene skal inneholde nødvendig informasjon for:
  - å utføre den statistiske analysen spesifisert i protokollen og statistisk analyseplan
  - å overvåke deltakerens sikkerhet
  - å gjennomføre studien i henhold til protokoll
  - å sikre dataintegritet og datakvalitet

Flere typer studiedata

Data generert/rapportert spesifikt for studien (primær datainnsamling/ aktive data)	Data hentet fra kilder utenfor studien (sekundær databruk/passive data)
via CRFer, laboratoriemålinger, elektronisk pasientrapporterte utfall PRO/PROM eller mobile/digitale verktøy	tidligere kliniske studier, nasjonale registre som dødsårsaksregistret og reseptregisteret, sykdomsregistre som kreftregisteret, og medisinske og administrative journaler fra rutinemessig medisinsk praksis



Data Integrity means that the **Data is managed the right way**

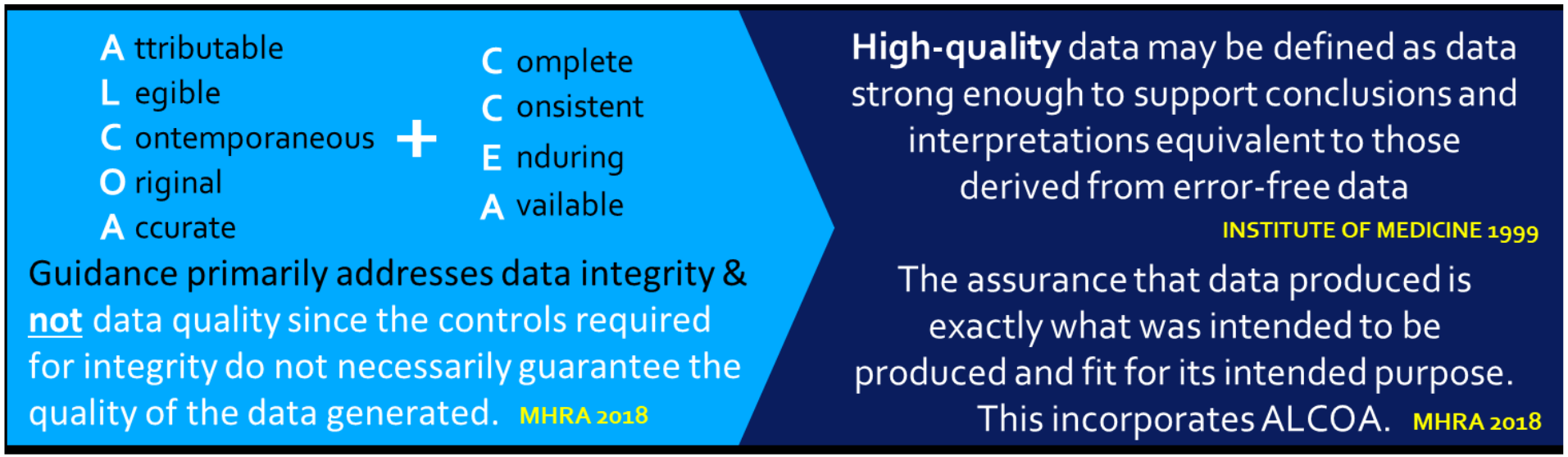
Data Quality means that the **Data is credible and reliable**

Dataintegritet

Data er håndtert på en riktig måte, dvs. at kravene til ALCOA og god dokumentasjon er oppfylt

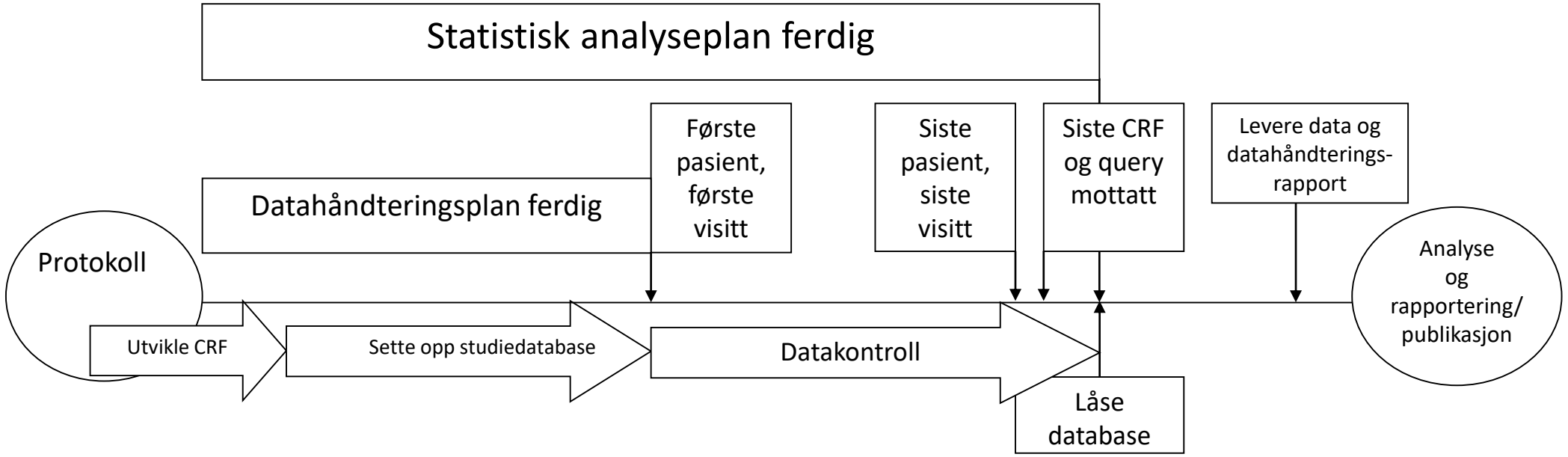
Datakvalitet

Data er troverdig og pålitelig. Data er egnet til formålet, vitenskapelig plausibel og pålitelig



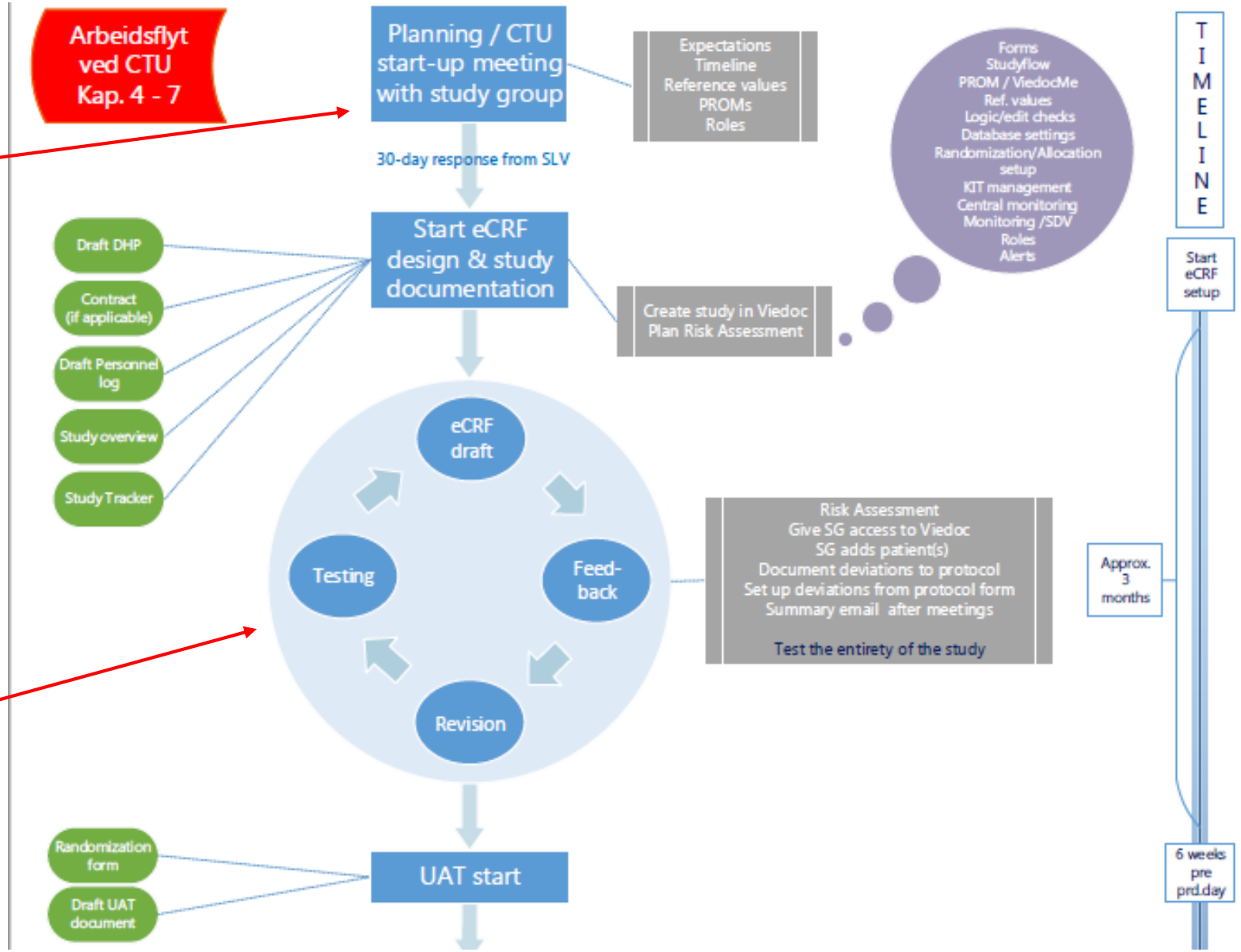
Dvs. kontrollere dataintegritet og sikre kvalitet på dataene vil bidra til troverdige studieresultater

Tradisjonell datahåndteringsprosess i en klinisk studie



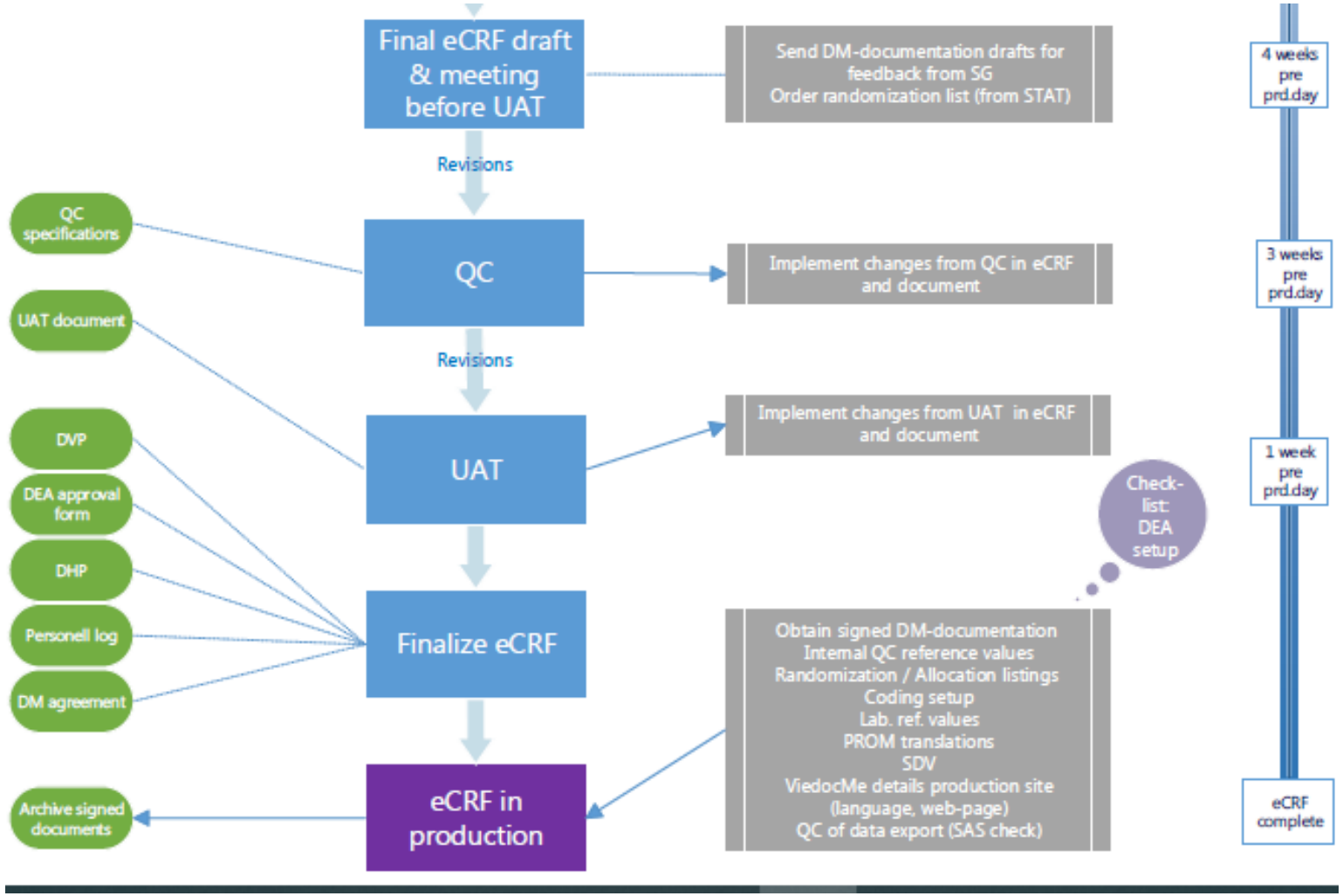
Oppstartsfase

- Tverrfaglig (TF) kartleggingsmøte
- Review av protokoll med DM perspektiv
- Legge en tidsplan
- En dedikert kontaktperson i SG
- Variabler og formater fra SG om mulig
- TF møter også underveis i utviklingen



Oppstartsfase forts.

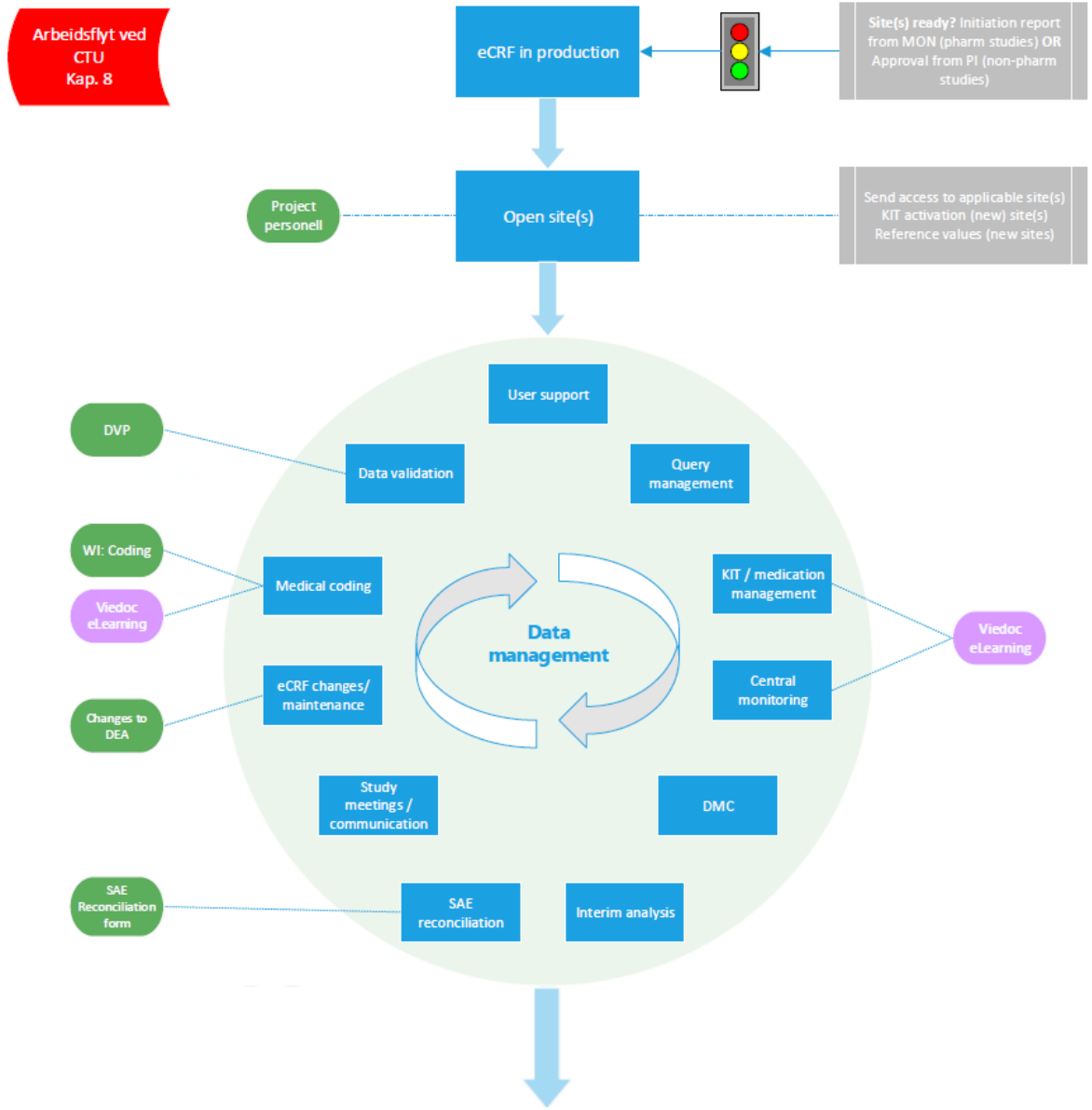
- Oversettelser av PROMs til andre språk, testet av brukere/SG
- TF involvering i UAT
  (User Acceptance Testing)
  - Statistikere- >primære /sekundære utfallsmål
  - Monitorer -> SDV og monitoreringsplan vrs valideringsplan
- Involverer QC av en annen datahåndterer
- Godkjenning av eCRF skal dokumenteres



Gjennomføringsfase

- Kan være korte eller lange studier
- Et eller flere sentra
- Nasjonale /internasjonale
- Komplekse utfallsmål -> utfordrende validering
- Safety rapportering til et eller flere legemiddelfirmaer med ulike krav til omfang og tidsfrister
- Interimsanalyser og leveranser til DMCer
- Koding av medisinske termer
- Randomisering med Drug Logistics, håndtering av legemidler fra produsent til site

- **Viktig med regelmessige møter med interne og eksterne i teamet!!!!**



Koding av medisinske termer

Her kommer AI/ML inn og
kan bidra til mindre bruk av tid og ressurser!!

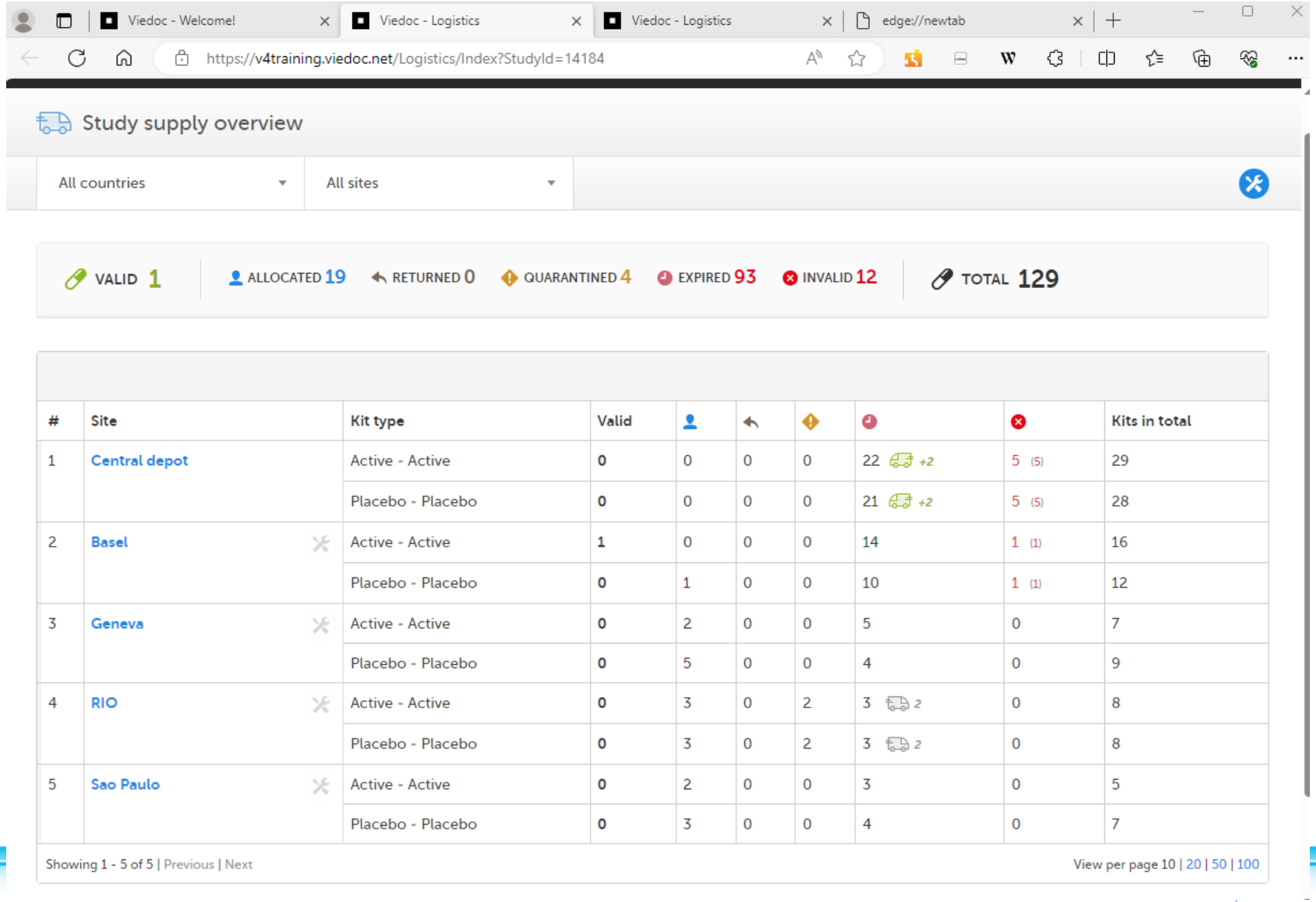
Incidence of Adverse Events in Individual Studies						
	Reported incidence by Treatment Groups					
SOC / Adverse event	Study X			Study Y		
	Drug X 60mg bid N=104	Drug x 30mg bid N=102	Placebo N=100	Drug x 60mg bid N=200	Drug Y 100mg qid N=200	
Nervous system disorders						
Headache	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)
Dizziness	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)
Gastrointestinal disorders						
Nausea	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)
Vomiting	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)
Flatulence	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)

Synonym	LLT	PT
Progressive headache	Headache aggravated	Headache
Worsening episodic headache	Headache aggravated	Headache
Light pressure on head	Head pressure	Headache
Head pressure in the morning	Head pressure	Headache

System Organ Class (SOC) (27)
High Level Group Term (HLGT) (337)
High Level Term (HLT) (1,737)
Preferred Term (PT) (23,088)
Lowest Level Term (LLT) (78,808)

WHO Collaborating Centre for Drug Statistics Methodology

Drug logistics



#	Site	Kit type	Valid						Kits in total
1	Central depot	Active - Active	0	0	0	0	22 +2	5 (5)	29
		Placebo - Placebo	0	0	0	0	21 +2	5 (5)	28
2	Basel	Active - Active	1	0	0	0	14	1 (1)	16
		Placebo - Placebo	0	1	0	0	10	1 (1)	12
3	Geneva	Active - Active	0	2	0	0	5	0	7
		Placebo - Placebo	0	5	0	0	4	0	9
4	RIO	Active - Active	0	3	0	2	3 2	0	8
		Placebo - Placebo	0	3	0	2	3 2	0	8
5	Sao Paulo	Active - Active	0	2	0	0	3	0	5
		Placebo - Placebo	0	3	0	0	4	0	7

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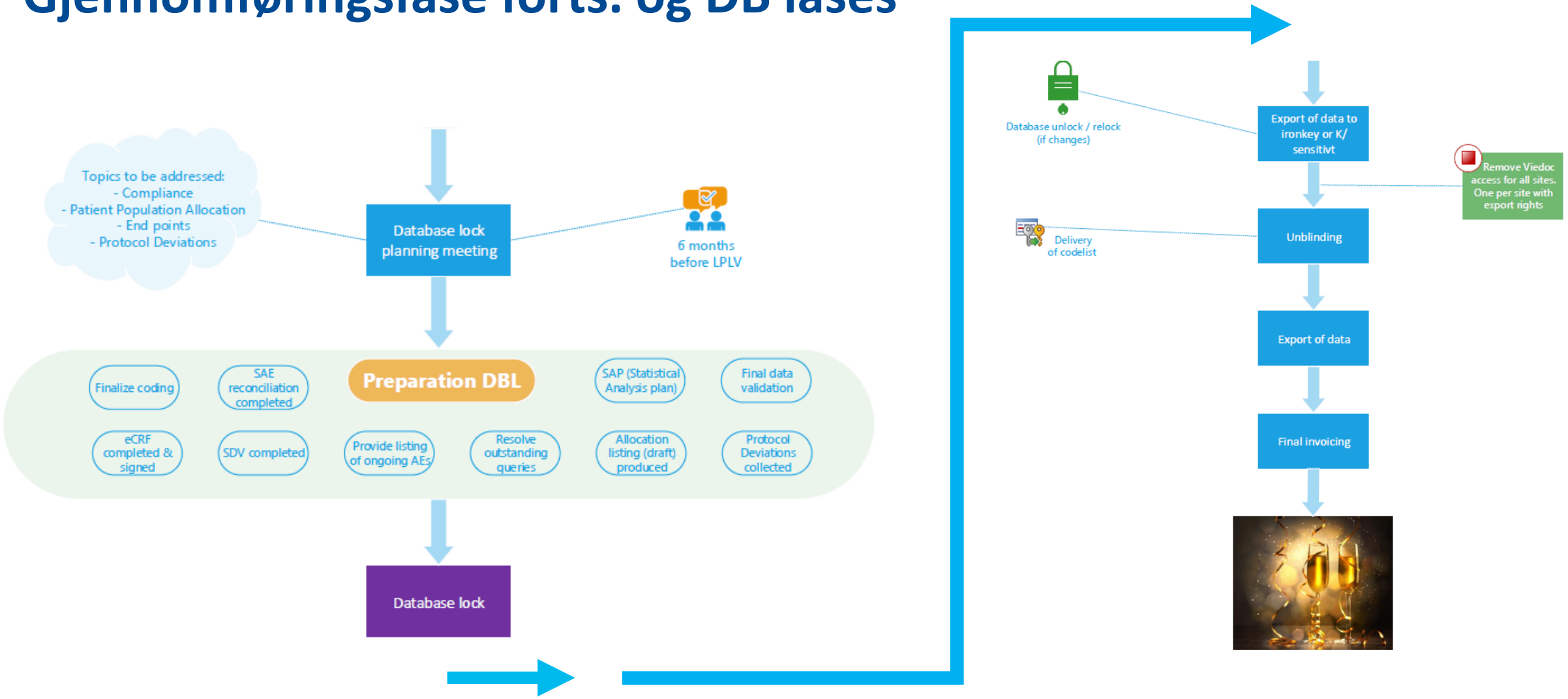
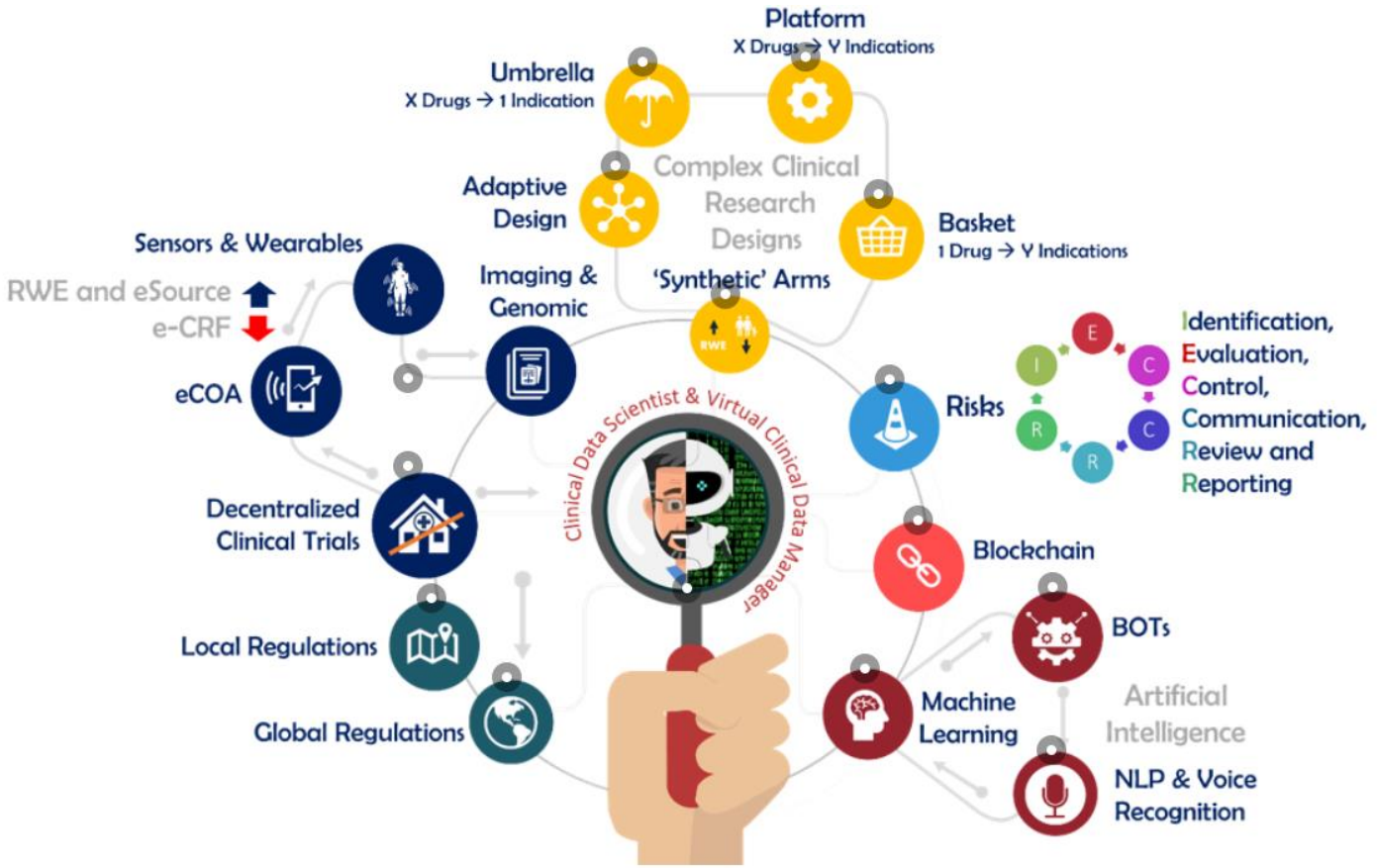
Gjennomføringsfase forts. og DB låses



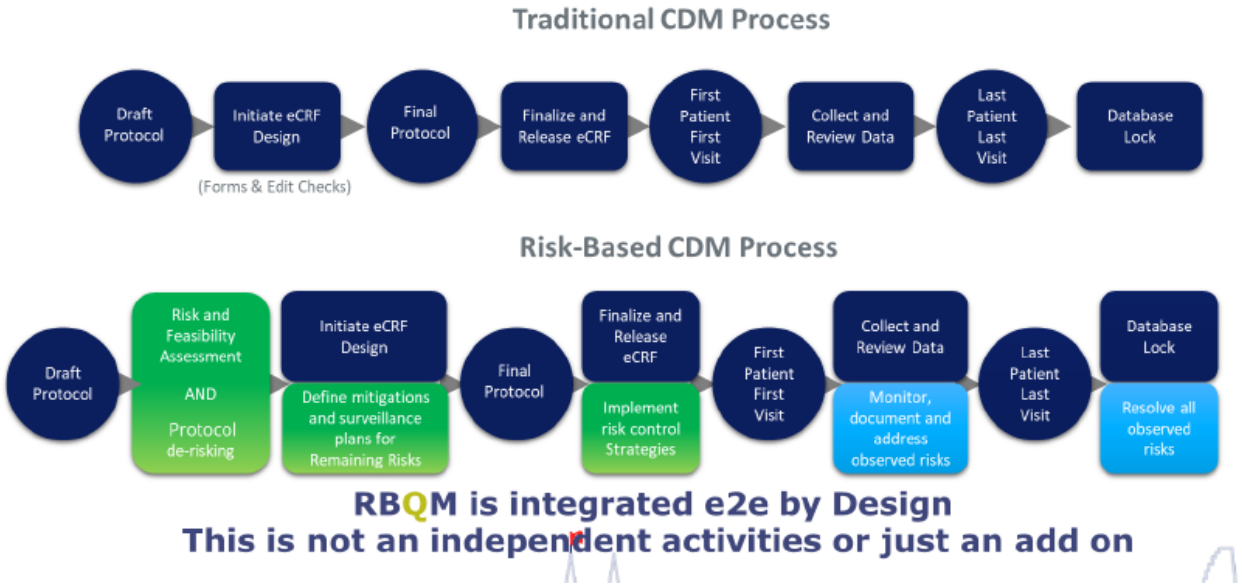
Hva er det nye innen faget datahåndtering?



https://scdm.org/wp-content/uploads/2022/03/2019_Evolution-of-CDM-to-CDS-Part-1-Drivers.pdf

Så utvikler prosessen seg med risikobasert tilnærming

E2e RBQM: On-Site, Remote, Central Monitoring and rb-CDM
Scientific and Operational Data Oversight: Workload, Audit Trail, etc.

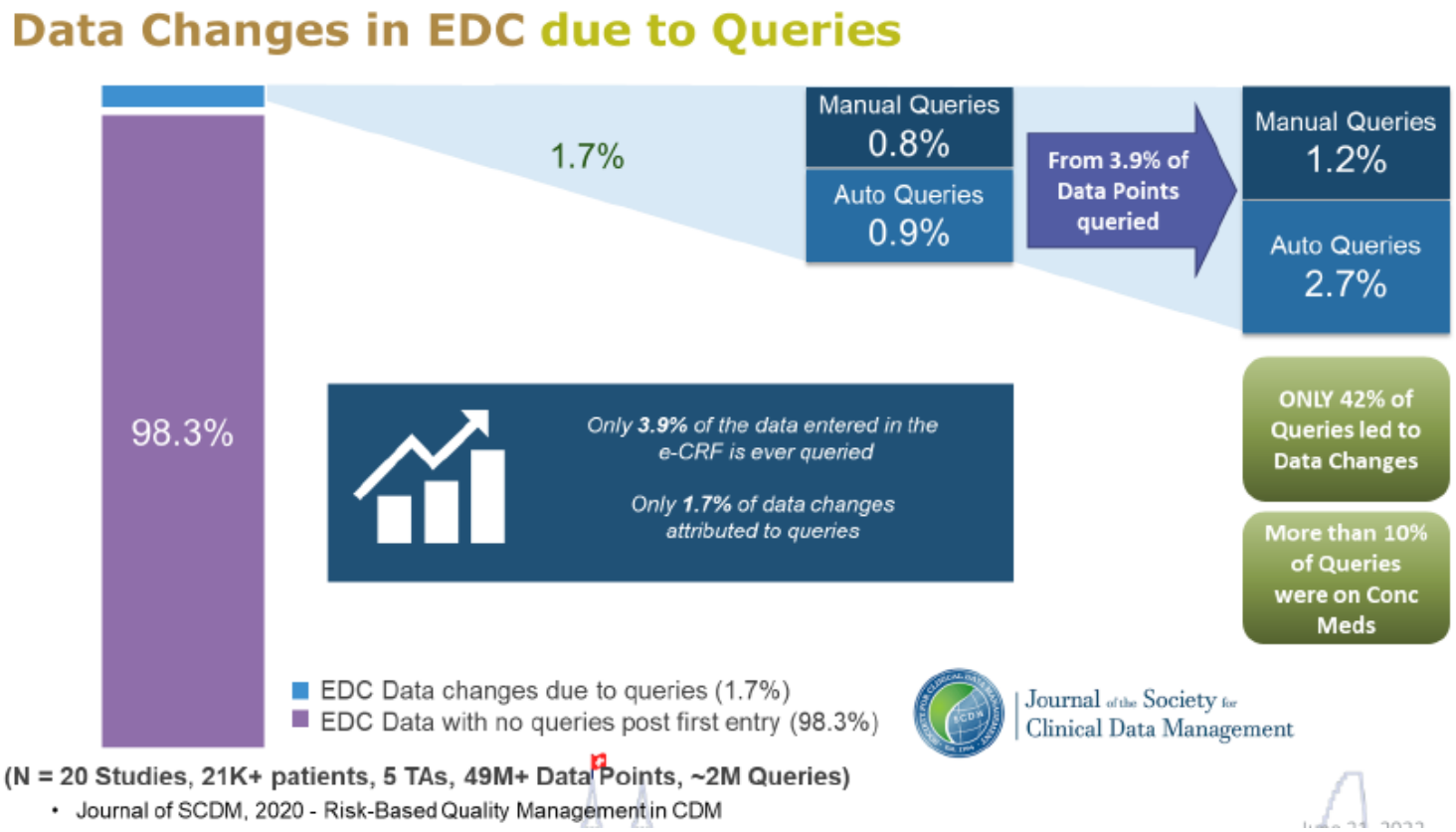


RBQM is integrated e2e by Design
This is not an independent activities or just an add on

SCDM-rb-CDM-July-6th.pdf

Hva får vi ut av tradisjonell validering?

Her kommer AI/ML inn og
kan bidra til mindre bruk av tid og ressurser!!



Sentral monitorering

- På tvers av studiedeltagere og senter i en studie, ved hjelp av målinger av indikatorer og bruk av statistiske metoder

Noen generelle momenter som gjelder for de fleste studier

- Hvor lang tid til besøk blir fylt ut
- Antall queries per senter, type queries, tid til besvarelse
- AE og SAE per senter og antall pasienter, husk normalisering f.eks. på tid i studie

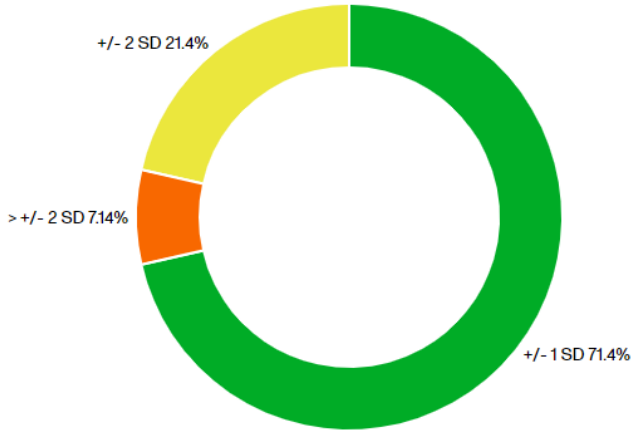
Studiespesifikke beregninger

- Varians og standardavvik av viktige variabler
- OBS: Skal ikke forveksles med interimanalyser og vurdering av effekt

Dashboard | Demographics | Adverse Events | Data Browser | Reports

Risk Indicators ↓ | by Key Risk Indicator ↓ | xlsx ↓ | Downl

e status for key risk indicator # of AE per subject



Select key risk indicator

- # of AE per subject
- Confirmed missing items per subject
- Unconfirmed missing items per subject
- Open queries per subject
- Closed queries per subject
- Rejected queries per subject
- Query response lag (in days)
- eCRF data entry lag (in days)
- Overdue events per subject
- Pending forms per subject
- Data changes per form
- Signature lag (in days)
- SFR %
- DQR %

Name	Country	Site Code	Site Name	Key Risk Indicator	Site Value	Study Mean	Study Deviation	Thresholds
ANT	Lithuania	14	Lithuania	# of AE per subject	0.57	3.69	1.41	
ANT	Norway	11	Levanger	# of AE per subject	5.20	3.69	1.41	
ANT	Norway	2	Ahus	# of AE per subject	5.16	3.69	1.41	
ANT	Norway	8	Førde	# of AE per subject	6.33	3.69	1.41	
ANT	Norway	1	OUS	# of AE per subject	4.43	3.69	1.41	

Indikatorer og toleranseverdier for kvalitet

Key Risk Indicators - spesielle faktorer for den enkelte studie

- Hva er kritisk i denne spesifikke studien?
- F.eks. antall **«Withdrawals (WD)»** og så definere QTL (Quality Tolerance limit) for denne indikatoren. Parameteren kan være **#WD, #WD/# included participant** eller **#WD/# participant visits**

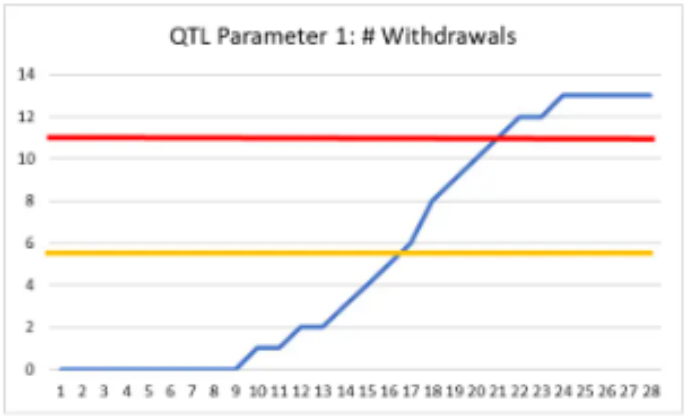


Figure 2a

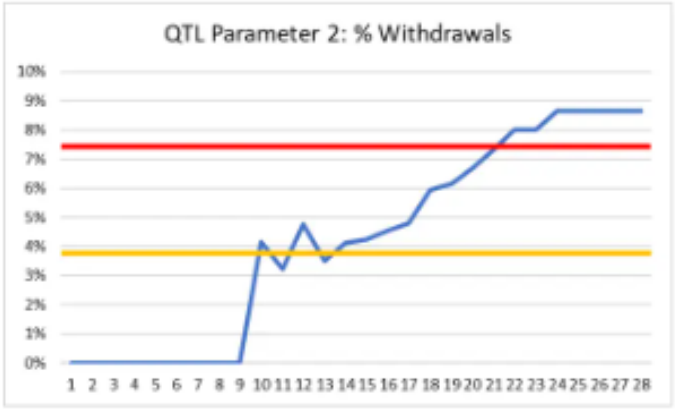


Figure 2b

[Defining Quality Tolerance Limits and Key Risk Indicators that Detect Risks in a Timely Manner: Reflections from Early Adopters on Emerging Best Practices (Part 3) (appliedclinicaltrialsonline.com)]

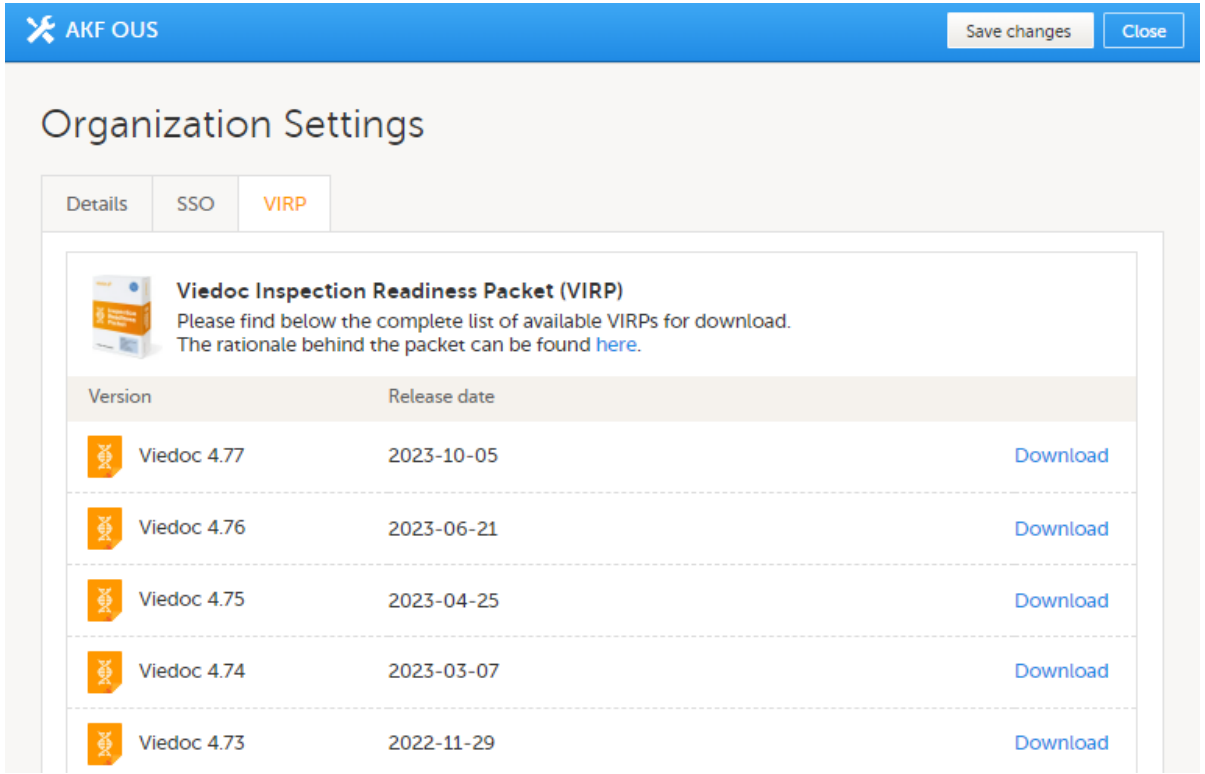
Regulatoriske krav til til DH og datafangstverktøy i LM

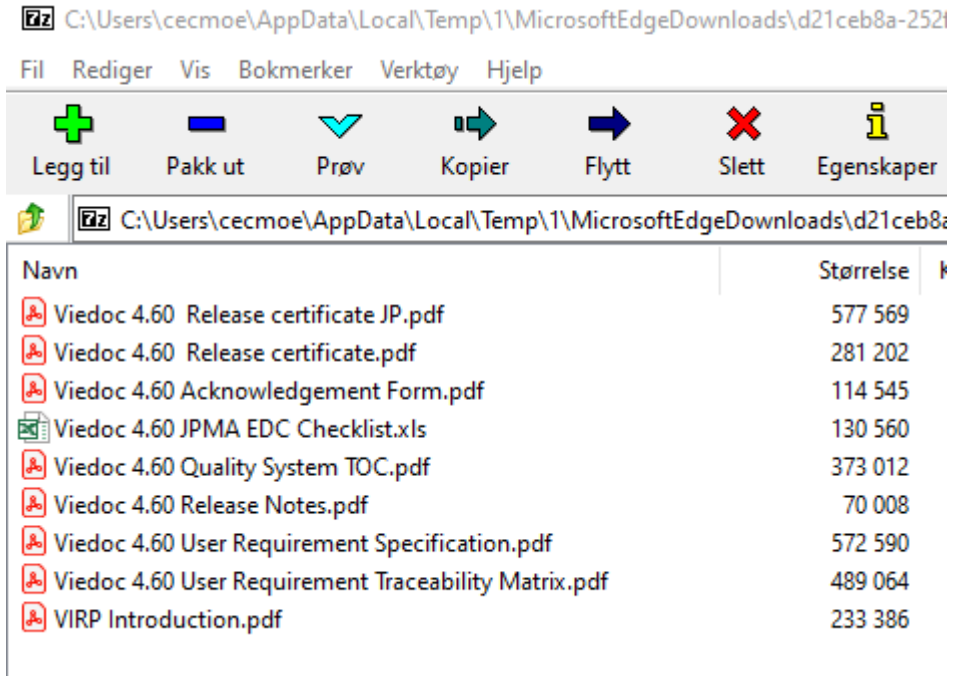
- GCP ICH R2
  - https://www.ema.europa.eu/en/documents/scientific-guideline/guideline-good-clinical-practice-e6r2-4-step-2b_en.pdf
  - Pålagt å ha er kvalitetssystem / prosedyrer
  - «Investigators copy» uten sponsors tilgang

- EMA Guideline on Computerised Systems and Electronic Data in Clinical Trials (erstatter PIC/S, kom I mars 2023)
  - Guideline on computerised systems and electronic data in clinical trials (europa.eu)
  - Inspection ready
  - Sponsor/hovedutprøver skal vite om leverandørens kvalitessystem/system life cycle

- eCF Requirements for Electronic Data for Regulated Clinical Trials
  - Downloads (eclinicalforum.org) Dette er en sammenfatning av krav, kan brukes som en sjekkliste

Krav til at Sponsor/hovedutprøver skal vite om leverandørens kvalitessystem/system life cycle





Litt ekstra om Viedoc

Future-proof

New updates are released regularly, all backward-compatible. No additional system validation is required for new releases.

Inspection-ready

Full documentation that meets inspection requirements, updated with every release.

The essentials

viedoc clinic™	For the investigator Manage all your trial data in one engaging solution
viedoc admin™	For the study manager Get your study started – and keep it running smoothly
viedoc designer™	For the study builder Create your own professional study – no advanced design or coding skills needed

Secure

All data is safeguarded using high-level security measures, including robust backup systems, advanced data encryption, and audit trails of all activity.

The addons

viedoc me™	For the subject Reliable data collection, directly from the source
viedoc connect™	For the decentralized trial Fully integrated support for Televisits and eConsent
viedoc logistics™	For the supply manager Smooth, secure and seamless inventory tracking and randomization
viedoc tmf™	For the sponsor Powerful documentation management on investigator and sponsor level
viedoc reports™	For the data manager Tailorable reporting for quicker, deeper insights

The essentials Viedoc Clinical

Electronic Data Capture	Features for collection, viewing and reviewing of CRF data in an ICH GCP compliant manner, including capture of binary data (images / documents) Sign data on form, visit or patient level Link data between forms (e.g. AE and CM) Laboratory reference values with time, location and factor scope
Medical coding	Feature supporting MedDRA, WHODrug B3- and C3-formats (certified by UMC) ATC classification system and IDF Batch coding Coding approval
Data review and cleaning	Data management review Clinical review Data lock on form, visit patient and study level Selective SDV on item level Role based query management
Randomization and allocation	Pre-computed static list or a dynamically generated / randomized list Individual and Global allocation lists RTSM (trial supply management in Viedoc Logistics)

Data export, API and metrics	24 / 7 output to Excel, CSV, SAS, PDF / A (compliant to FDA submission, eCTD) and CDISC ODM formats Scheduled exports Online data preview and chart visualization API for import and export of data in CDISC ODM Real-time metrics on data quality and performance
Training and certification	Online documentation and eLearning (documents, links, videos) Certification with automatic creation of user diploma User logs (PDF and Excel)
Messages	Email alerts for data events, data status and milestones Local-language SMS / text messages / reminders sent to subjects
Other	ISO 27001 compliance Two-factor authentication SSO (single-sign-on) Support for eSource DDC Multilingual Regulatory compliance – EMA, FDA, JPMA, CFDA Compliance with personal data protection laws – GDPR (EU), APPI (Japan), HIPAA (US), PISS (China) Audit trail and electronic signatures compliant with FDA 21 CFR part 11 Contemporaneous and independent investigator copy created at each CRF save Support for simultaneously running unlimited versions of a study configuration

The essentials Viedoc Admin

General study maintenance	Role delegation service
	Study level database lock feature
	Study-recreation from a previous snapshot (CDISC ODM)
	Unique and fully self-service study decommissioning feature including status reports and archiving recommendations
	Documentation and certification management
	Assignment of study designs
	Study settings
	Study license management
	API management
	TMF management
	RTSM management
	Reference data management
	Medical coding dictionary management
Site and user management	Site creation, with code, time zone, type (production / training), recruitment metrics
	User management, with invites, resets, and removals
System / organization management	System user management
	SSO configuration
	VIRP (Viedoc Inspection Readiness Packet)

The essentials Viedoc Designer

Study building	Drag-and-drop form design with more than 18 different item types to choose from
	Form preview allowing the designer to verify layout, conditions and checks directly onscreen
	Automatic creation of blank and annotated CRFs
	CDISC CDASH form library with over 20 ready-to-use forms
	Ready-to-use study templates in CDISC ODM XML format
	Form translator for managing multiple study languages
	Best-in-class support for complex study designs/requirements
Version management	Seamless support for mid-study changes due to protocol amendments, updated requirements or adaptive trial design
	No migration of data like in other systems
	Support for simultaneously running unlimited versions of a study configuration
	Transportability / import / export and off-line examination / revision of the configuration in CDISC ODM XML format
	Automatic creation of abbreviated and complete study configuration report
Conditions / Validation / Logic	Support for configurable responsive / interactive visibility conditions on a role-, study schedule- or data dependency-level
	Automatic design validation upon publishing a study design
	Java script expression editor for faster, more high-quality code
	Support for configurable calculated values (close to unlimited in algorithm complexity level)
	Realtime field-level edit checks, cross-form checks and data derivations
Value added services	Custom study build services
	Study build certification