

Abstract

Novartis Vaccines & Diagnostics (NVD) has been using several central servers to store, analyze and report clinical trial data, and has in its archives data from a multitude of studies (~ 400) run over the past twenty years. There is an increasing need to query or analyze aggregated data from many trials instantly for a variety of reasons, such as safety signaling, data mining and answering questions like the incidence of reaction X in all trials you ever did (including ongoing trials) with vaccine Y and/or adjuvant Z.

In order to address this challenge NVD decided to implement a Clinical Data Repository where all relevant historic trial data (recent and old) will reside and data from ongoing trials will be collected in a near-real time fashion.

As a result of this exercise, a revolution is currently in the making: a new 'hub' environment has been chosen and implemented, processes re-engineered, and a series of CDISC data standards have been adopted. These changes will involve not only future studies, but also all the legacy ones, which then need to be converted to the new standards.

Introduction

The Clinical Data Repository (CDR) initiative represents a major transformation of the entire landscape within Data Management and Biostatistics and has far-reaching value for the entire Development organization. The CDR program was immense in scope – comprised of seven large sub-projects. Project execution was guided by a company-wide methodology

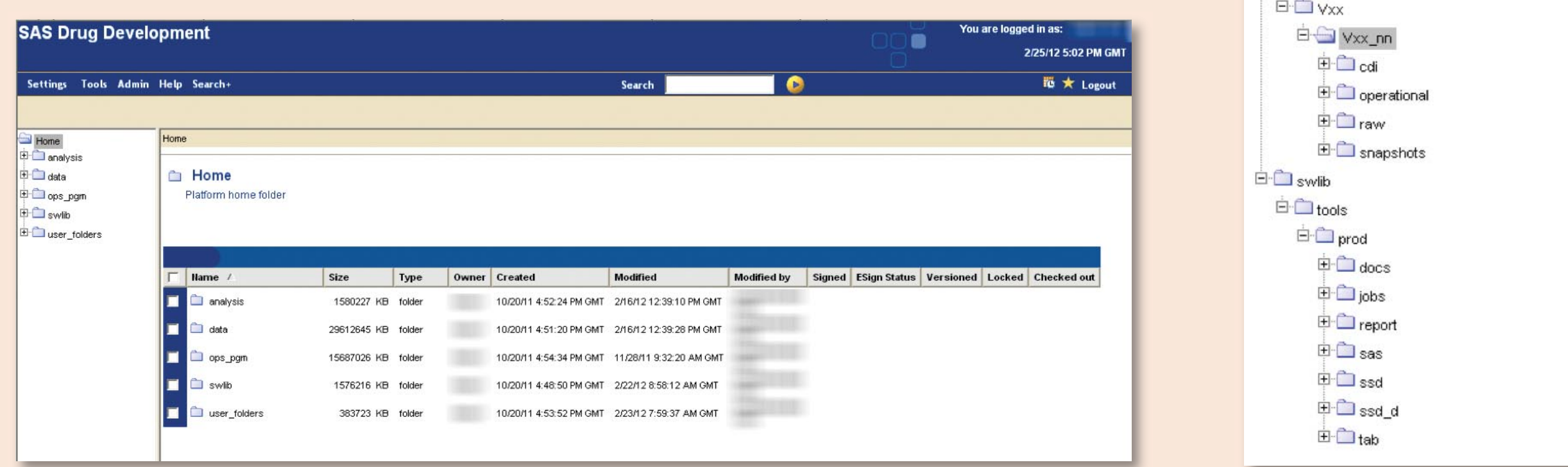
SEVEN SUB-PROJECTS WITHIN THE CDR PROGRAM

- 1 Install and customize SAS® Drug Development (SDD) as the "hub" environment
- 2 Define a new CDISC-based data standard (ODASH/SDTM)
- 3 Build interfaces to SDD for feeding data
- 4 New coding system for adverse events, histories, medications
- 5 Re-engineer processes by re-writing SOPs and work procedures
- 6 Migrate approximately 400 legacy studies to CDISC data structure
- 7 Migrate SAS reporting application library (macros) to SDD

Selecting solution and planning

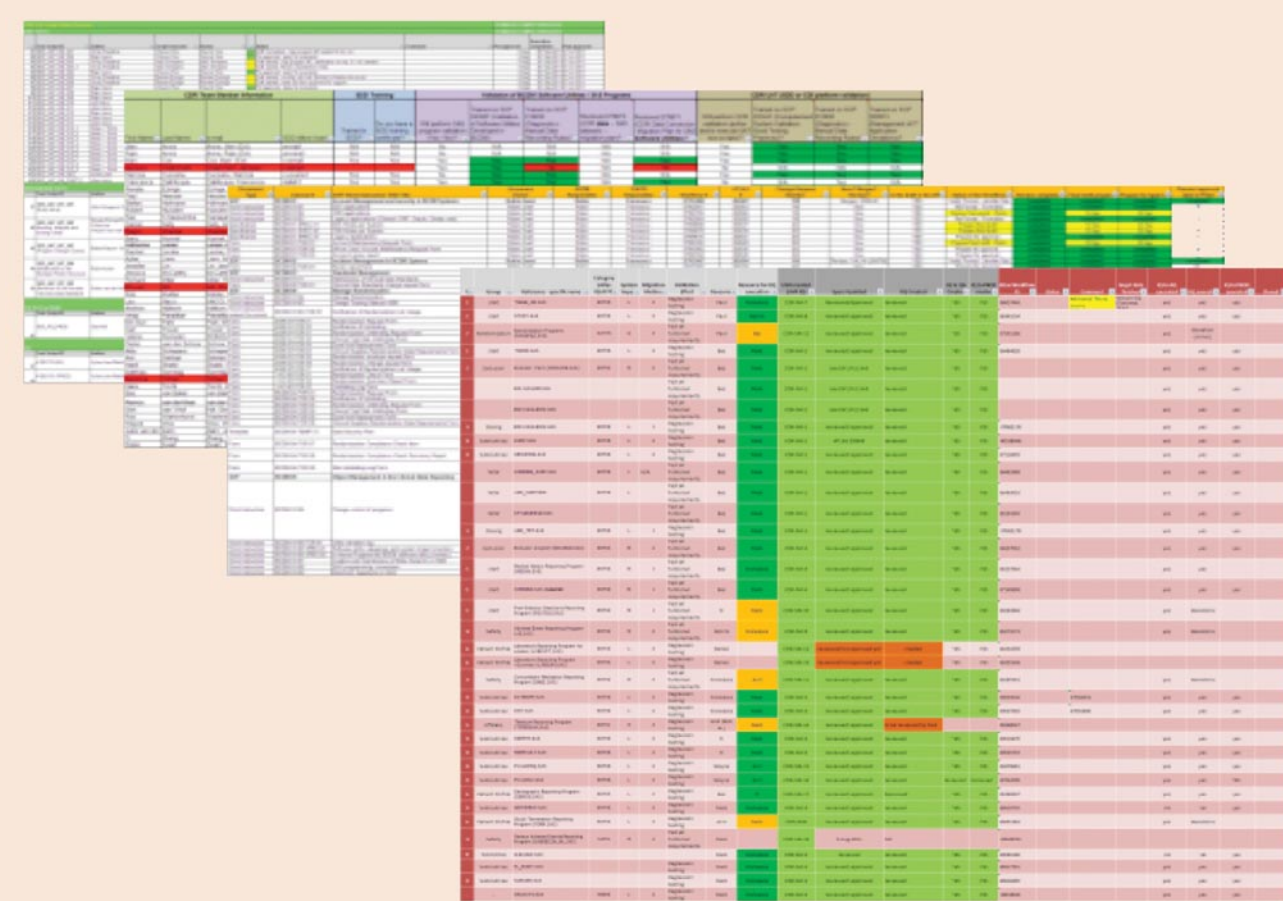
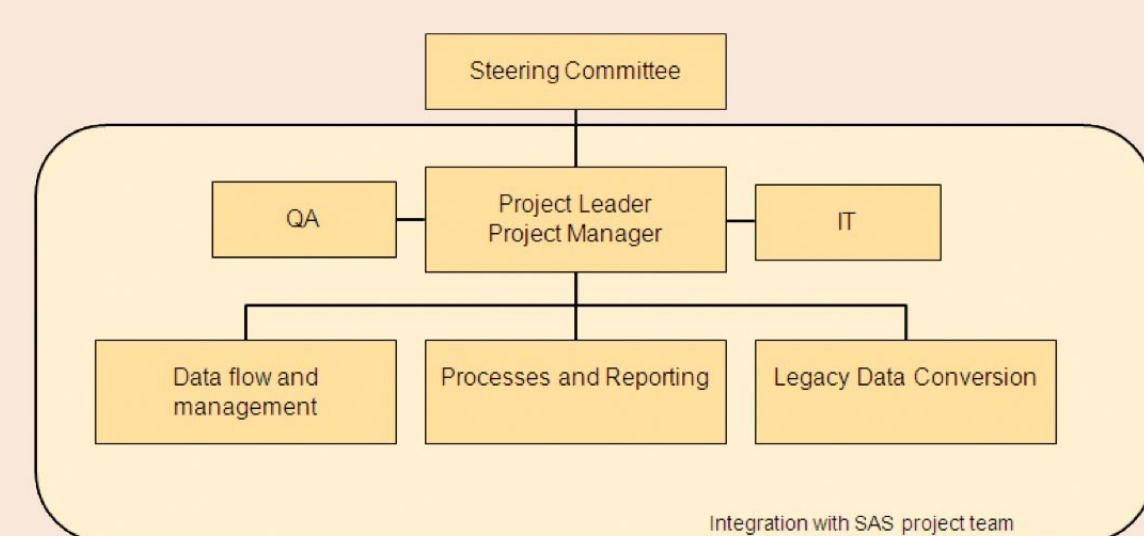
SAS® DRUG DEVELOPMENT

SAS Drug Development was chosen as the "hub" environment. It is centrally-hosted in a SAS data center, is scalable, and has a feature set that facilitates establishment of a controlled environment for data storage, data management, and statistical computing.



PLANNING AND MONITORING

The project was to be completed in approximately one and a half years without a pilot phase. Such scope and timelines required an equally grand planning effort around a solid team structure. In the end, there were several project plans comprising > 2000 lines.

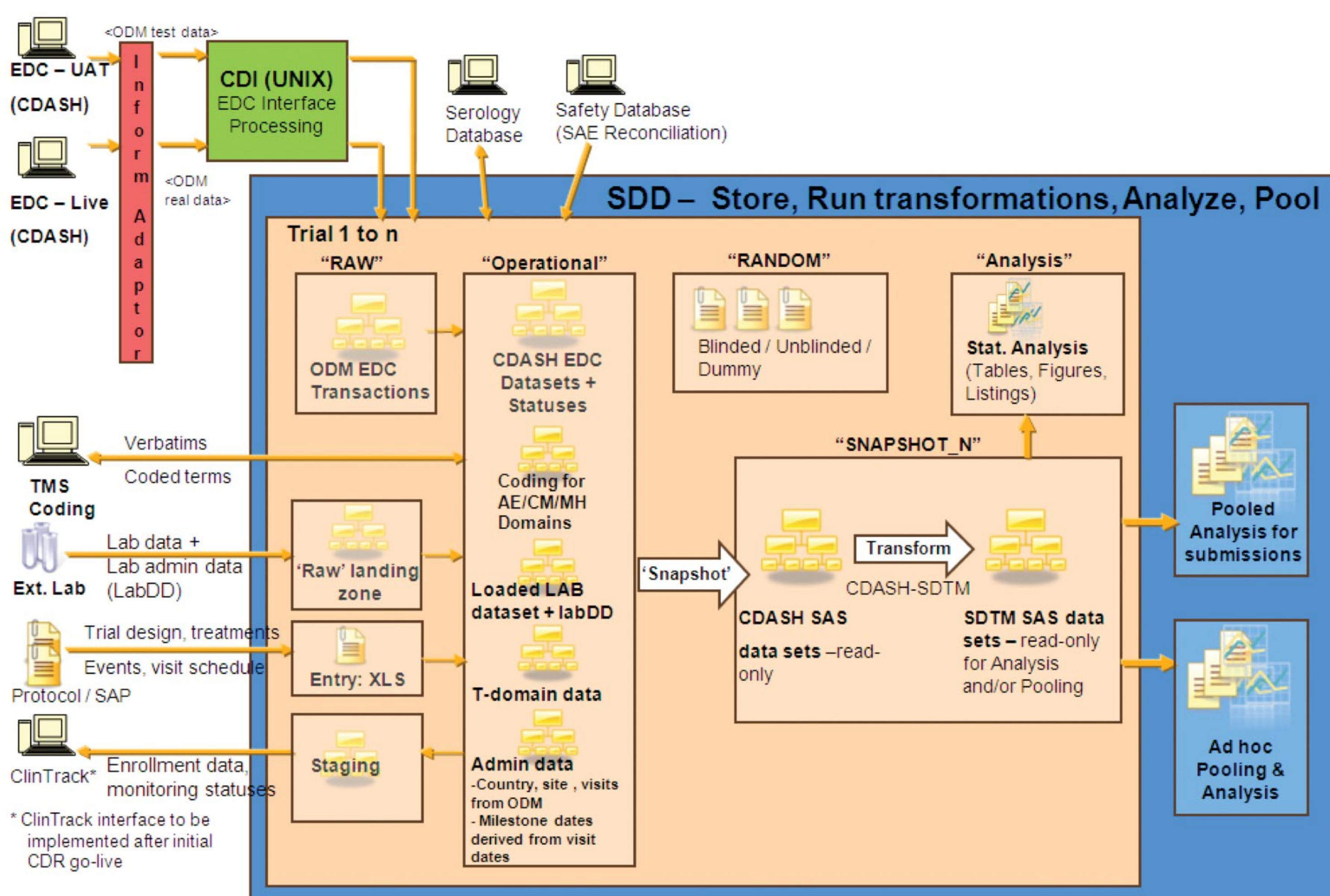


KICK-OFF
AUGUST 2010

ORGANIZING A TEAM, MAINTAIN MANAGEMENT SUPPORT, GETTING RESOURCES

A large project involves many people. Challenges include sustaining motivation, focusing on goals, keeping schedule and ensuring good communications, mitigating risks. Continual executive support is crucial, and securing adequate resources is vital. All of this requires good project leadership.

CDR Data Flow



Business drivers

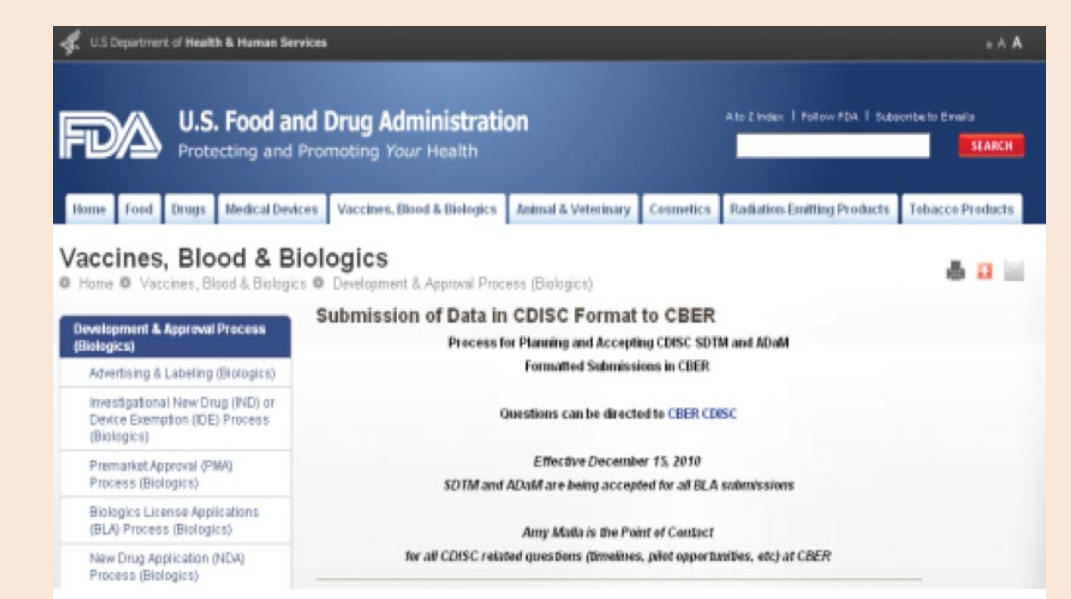
ANSWERING HEALTH AUTHORITIES

- Increasing numbers of requests from Health Authorities worldwide
- Increasing complexity needing data from across trials and products
- Expectations of proactive safety signal detection and analysis
- Responses expected within very short time intervals



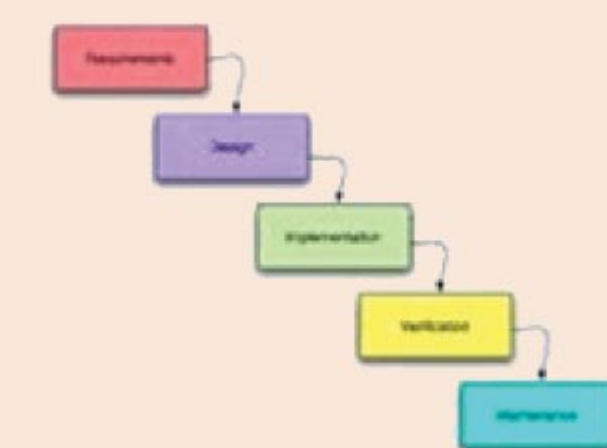
ADOPTING INDUSTRY DATA STANDARDS

- Industry speaking in CDISC terminology
- Regulatory authorities accepting and soon requiring CDISC data submissions



MODERNIZE THE SYSTEMS AND PROCESSES

- Coding of adverse events, medical histories, concomitant medications can be optimized
- Additional functionality required for controlled SAS programming environment
- Legacy processes needed update to scale with business realities
- Concerns for disaster recovery and business continuity



Implementation

Summary: A recap of each sub-project reveals many achievements realized by smart and hard-working teams of people

ESTABLISH SDD AS HUB

- Computer system validation
- ~4700 pages of validation documentation
- Three environments (DEV, TEST, PROD)
- Processes and mechanisms established for post-go-live support
- Over 100 users trained and accounts granted
- Multiple modes of access (desktop, terminal server)
- PC SAS available to power users



NVD CDISC DATA STANDARD ESTABLISHED

- SDTM 3.1.2 used as the foundation
- 19 of 30 standard domains employed plus 5 "custom" domains
- CDASH data standards employed in data collection
- Mapped ~450 fields from both Legacy data standard to SDTM and CDASH to SDTM
- Mapped ~4500 codelist entries
- All new trials beginning from June 2011 using CDASH data standard



DATA INTERFACES ESTABLISHED

- Extremely complex EDC-to-SDD interface coded from scratch
- Interfaces designed for high volume and high frequency data transfers
- TMS interface created to enable use of new coding paradigm
- Multiple database connections made requiring extensive firewall configuration
- 107 VPN connections linking 2 data centers



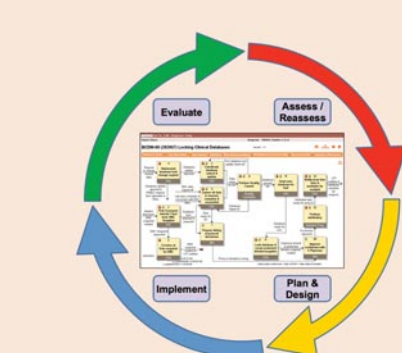
NEW CODING SYSTEM

- Updated MedDRA and WHODrug dictionaries
- Retired ICD-9 for coding medical histories
- Fully validated system
- Shared system with Novartis Pharmaceuticals division



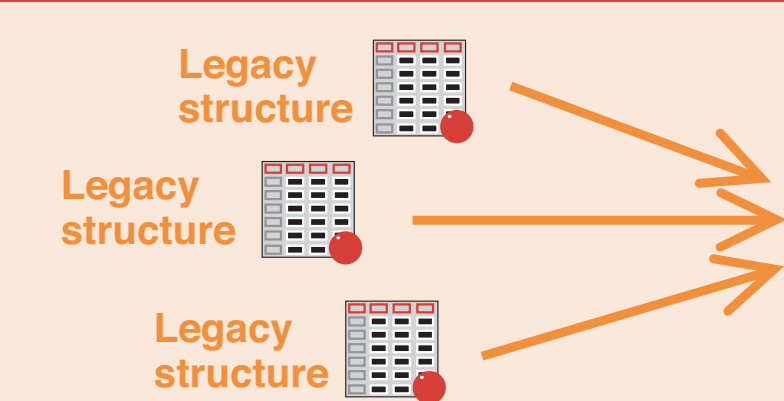
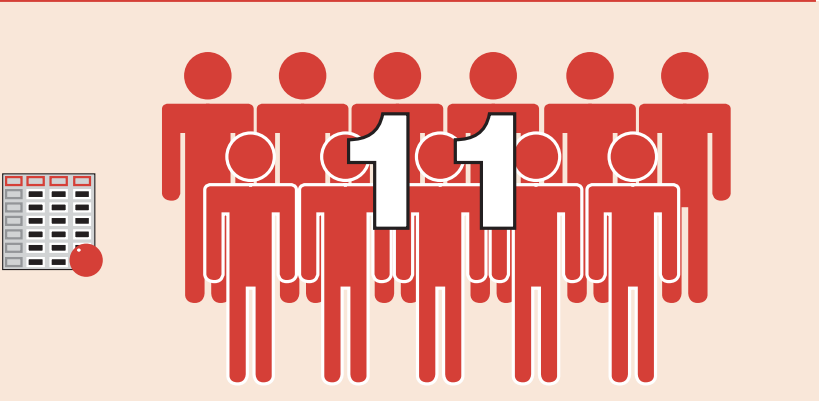
NEW SOPs, WORK INSTRUCTIONS

- Business process re-engineering
- 100 controlled documents created/reviewed/revised
- 13 SOPs
- 20 Work instructions + 6 related documents
- 52 Forms, 7 Specifications, 2 Templates



CONVERTING ALL LEGACY DATA

- First of two phases nearing completion
- 153 studies spanning 19 years and >76,000 subjects
- 2,837 SAS datasets with >245 million data points
- NVD developed 56 migration programs
- T-domains involved >300 Excel files completed by >100 clinical and BCDM people



PORT THE SAS STANDARD SOFTWARE LIBRARY

- 39 programs belonging to Statistical Reporting
- 16 programs belonging to Data Management
- Programs can be thousands of lines
- Made to work with SDTM data structure, SDD, and updated output layouts (RTF, PDF)
- Full validation of each updated program



KEY CONCEPTS APPLIED AND LESSONS LEARNED

- It always takes more time, effort, and people than you originally think
- Allow for thought time and trial-and-error when trailblazing
- Dedicate people to the project instead of trying to work on daily activities in parallel
- Bring in expertise when needed
- Lay out the project ground rules early and enforce them
- Establish a common project-oriented mindset among team members
- Fully integrate vendor and other external project team members
- Recognize and address the challenges of a geographically dispersed team
- Manage and prepare people for change



GO-LIVE
DECEMBER 2011