Science For A Better Life

Metadata based Architecture for E2E support of Clinical Development processes

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Metadata based Architecture for alignment of Clinical Development processes

- Standardisation as required prerequisite for process alignment
- Architecture considerations for E2E Processes
- Scope of a Metadata registry
- Conclusions

Metadata Models are requiring standardization

Standardization is seen as a key success factor and competitive advantage for an efficient set up, study conduct, analysis and reporting of clinical trials, projects, and all submissions as well as reporting requirements beyond submission.

Goal is to maximize the automation of deliverables as far as possible with highest quality.

Ease of data integration within -and if required- across projects, in order to be able to instantaneously react on analysis requests from internal and external parties.

Standards and their mapping rules enable faster ownership of acquired projects

Metadata Models / Global Medical standards

Global Medical Standards (GMS) are key components :

of operational efficiency

For industry compliance

For output agility across many Development functions.

Operational efficiency - defined as the speed with which clinical study data can move through the protocol driven data collection/management/analysis and reporting processes is largely dependent upon the effort needed to implement these processes.

GMS define the common language with which the functions can communicate across theses processes within the organization and external to the organization

An effective set of processes and workflows supported by an efficient system will overall support this optimization and are essential for long-term operational success

Industry and regulatory requirements

The pharmaceutical industry is required to adopt to the now mature Clinical Data Interchange Standards Consortium (CDISC) data standards.

The usage of CDISC standards enables cooperation across functions and systems transferable via the ODM XML format which many vendors, partners and CROs will eventually (1-3 years) comply with.

Any standards implementation needs to reflect on CDISC standards as **output** format,

should also be reflected in internal workflows as far as meaningful to allow seamless transition and extradition of data and to base internal analyses/ reports on the same data architecture as agencies require to see.

Recent CDER requirements include traceability requests- towards SDTM and ADAM data models.

To cover future requirements from the FDA and EMA (and others) the future system will also be required to ensure version management for these standards

Standardization as an enabler for internal requirements

Recent demands for data output (reports, analyses, data transfers, etc.) has expanded the demand on clinical data processing.

The agility with which an organization can produce such output is dependent upon access and consistent organization of the data needed for the output.

GMS maintenance supported by a system will support this access by providing a common organizational understanding of the data structures and content thereby facilitating the definition and provision of output.

Reliability of output will be another main driver of this implementation.

Why Medical Standards?

Objectives of Standards:

- Provide a reliable framework for processes and defined workflows
- Support an efficiency and quality driven Clinical Project Standards development
- Reduce redundancy and increase within and across project consistency
- Enable consistent processes
- Reduce reinvention of metadata and processes
- But: be flexible enough to meet project needs
- Release teams from administrative tasks
- Support Medical Governance
- Support Sponsor governance:

Provides a reliable and consistent framework for specifications to CROs and is enabler for control of compliance and quality

Scope of Standards

- CRF and eCRF (e.g. CRF completion guidelines)
- Database structure (SDTM, ADAM) + process required elements
- Items with associated code lists, labels and formats,
- Edit check specifications
- Calculation rules
- Standard laboratory Analyte table (including conversion factors for different units)
- Medical review standards (different from statistical tables)
- Tables, listings, graphs (including process support)
- Protocol templates
- Clinical study report templates
- Clinical Summary templates
- And more…

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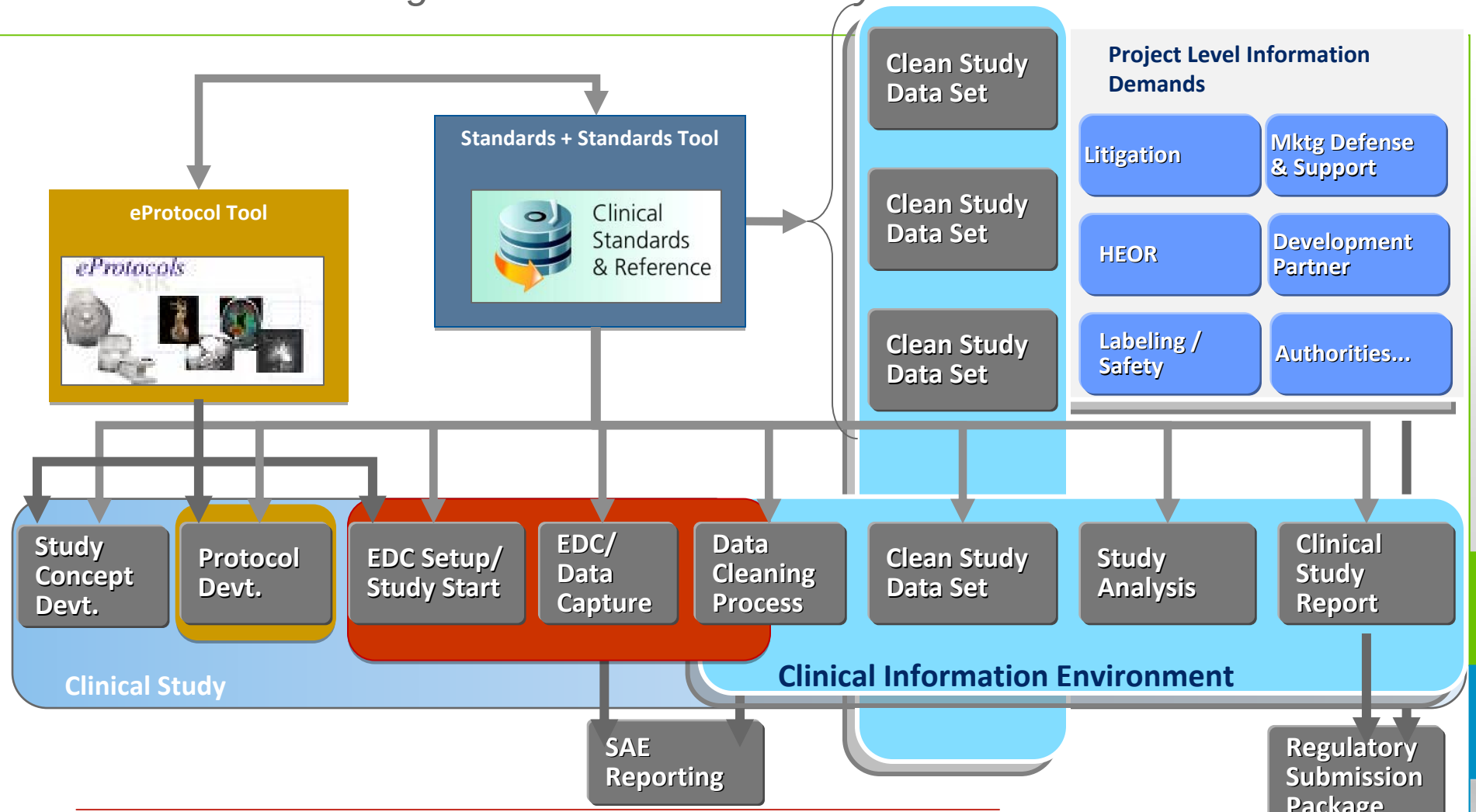
General System Architecture

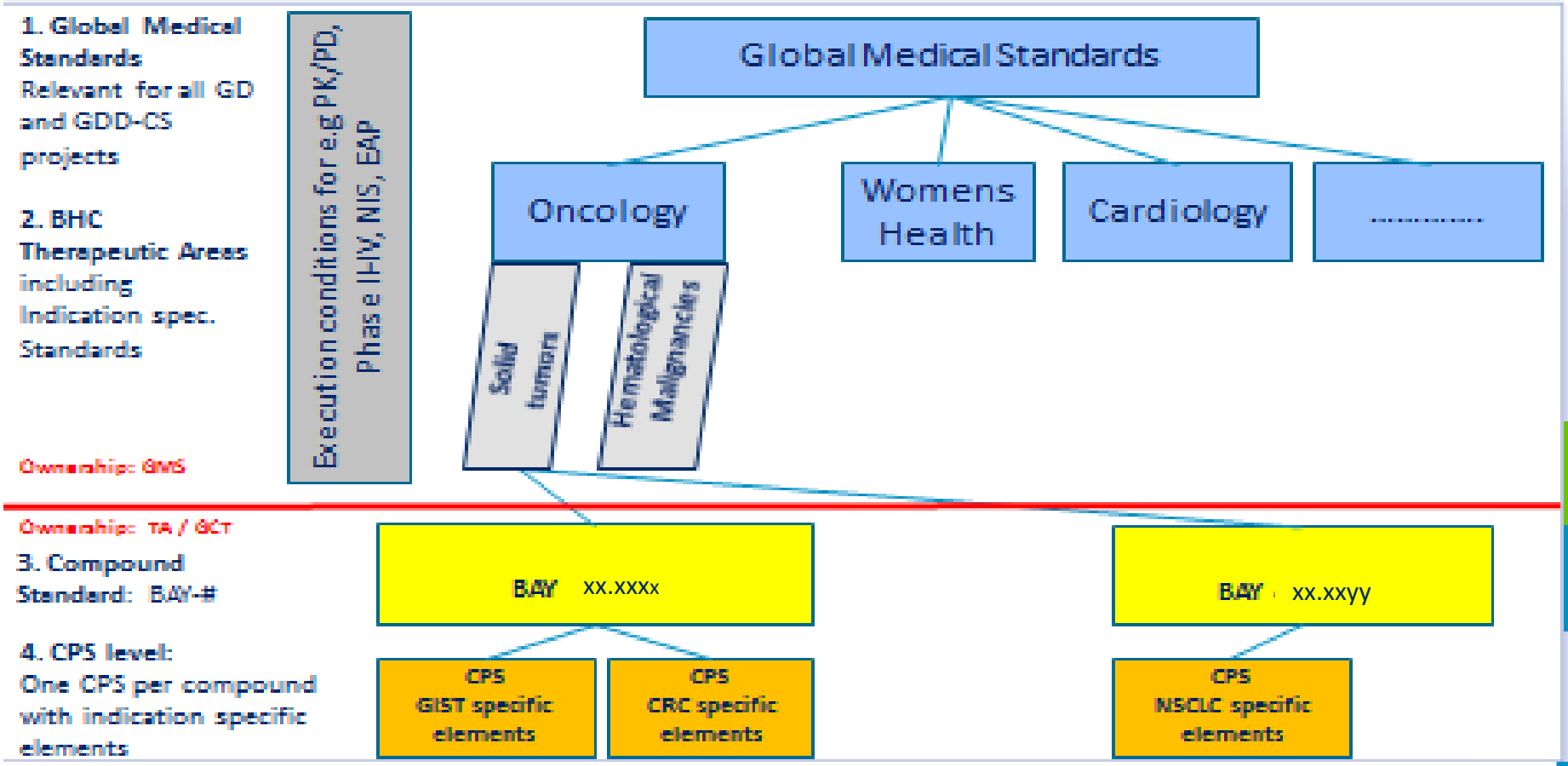
Underpinning productivity enhancements from study set up and conduct through to submission and beyond



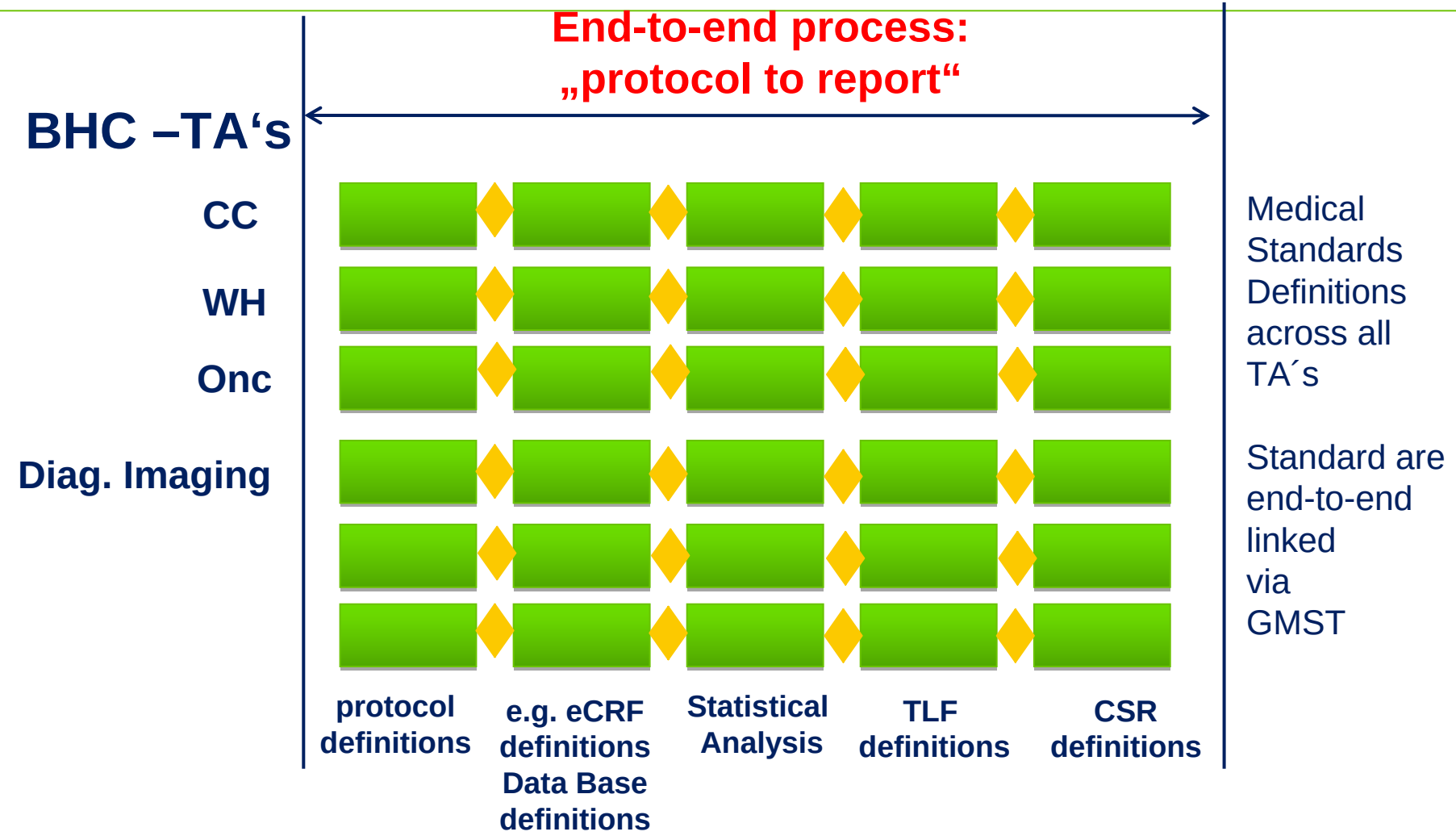
EDC = Electronic Data Capture; SAE = Serious Adverse Events; HEOR = Health Economics Outcomes Research

Global Medical Standards

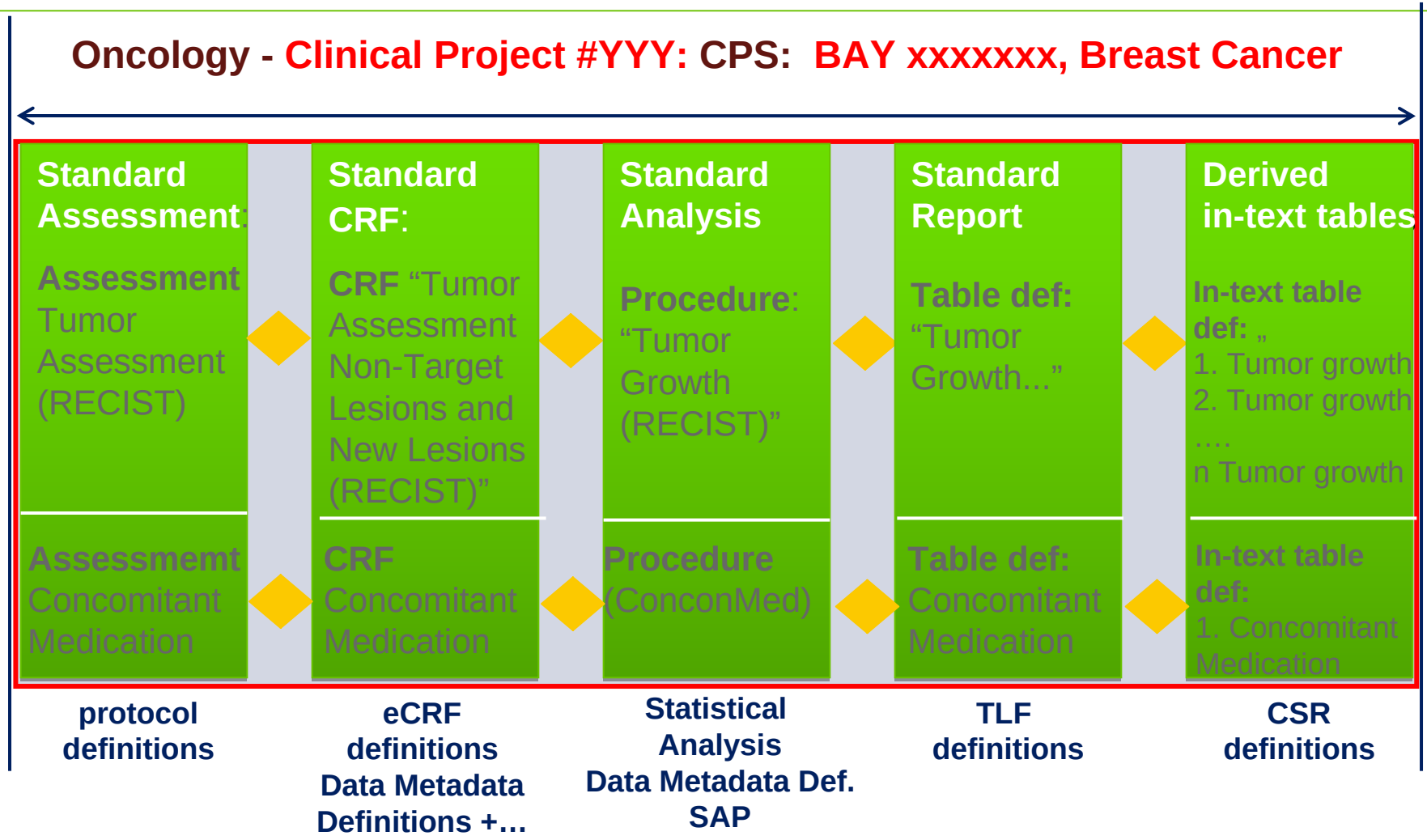
Hierarchy



GMST Medical Standards
interlinked medical standards



Example:
Interlinked Medical Standards in GMST
- high level concept based on Oncology trial



Example:
eProtocol Tool

Business need: Protocol Design process

- Need to reduce large percentage of **protocol amendments prior to the First Patient First Visit (FPFV)**
- Need to reduce number of **re-feasibilities**.
- Need to reduce number of CRO contract change orders due to
  - **late changes in study designs of outsourced trials**
  - **inconsistent use of medical standards**
- Need to reduce amount of data points being captured that are unnecessary

- Need direct (electronic) access to medical standards
- Need to use structured protocol approach to fully realize E2E efficiency goals

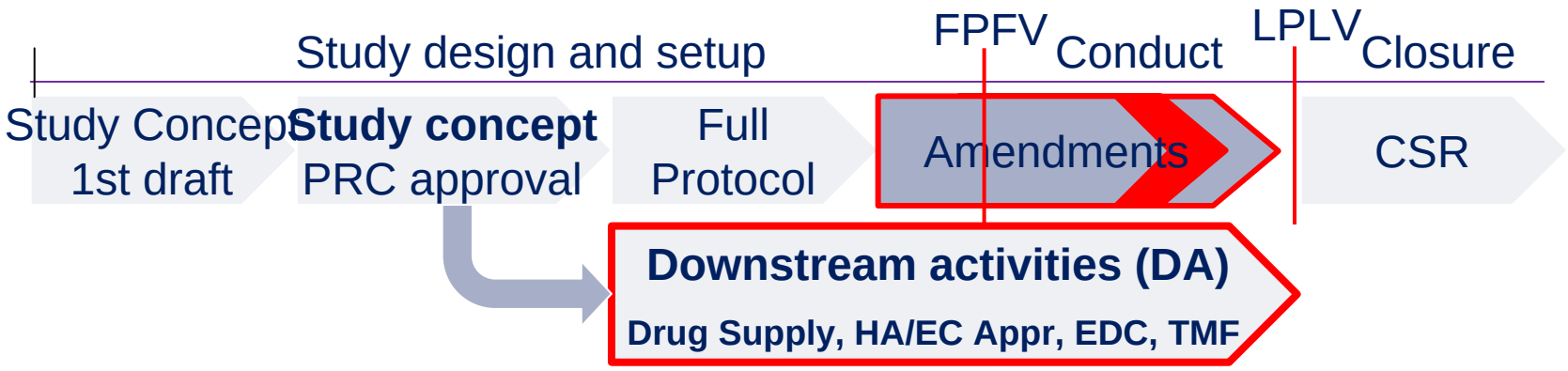
Gartner: CDISC standardization

- 80% of all benefits derived from Standards **occur in the study startup phase**

eProtocol tool identified as key enabling technology

Example:
eProtocol Tool

1. **Efficiencies are realized** due to the following enhancements:
    1. Structured and standardized protocol
    2. Downstreams are executed consistently at the earliest point in time
    3. E2E-standardization based on the new CPS process in GMST



Example: Creation of eCRF based on standard CRF´s

CRF's will be standardized and transferred to EDC for execution in trials

- GMST captures all specifications of all Standard CRF´s
- CRF specification cover:
  - All mandatory and optional domain variables
  - All edit checks , CRF instructions, help text etc.
- CRF's are related to either Global, TA-level or indication level if needed
- CRF's will be completely specified and stored in GMST (study level definition)
- Compiled CRF is ready for transfer and execution in EDC for production

Process of Standard CRF specification in GMST and execution/ compilation in EDC

- GMST Meta model to be developed for CRF's
- CRF's will be entirely specified based on ODM Meta model in GMST
- Transfer into EDC Test study Formatting and –compilation ?
- Store and relate CRF-compilation to CRF specification in GMST (Global or TA level)

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Scope of a Metadata registry for Global Medical Standards

Supports all the objectives of standards listed above in a consistent manner

Generates efficiency through electronically executable defined elements or linkages to and between peripheral systems for all supportable workflows

Builds consistent structured workflows for development and maintenance of standards

Builds controls for adherence and reports on deviations

Reduces redundancy in maintenance of elements by linkage to source as long as no confirmed deviation is required

Enables reliable version management

Supports mapping between versions and legacy standards or standards used in acquired projects

Global Medical Standards Tool - processes

Workflows will support the build and change management of standards (incl. promotion, cascading)

Global medical standards maintenance process:

all steps in the system for developing new standards, retire or change existing standards on GMS, TAS, Compound, Clinical project (incl. promotion of standards)

CS/CPS development process

all steps in GMST for set up and maintenance of Compound/Clinical projects

Medical standards governance process

all steps in GMST for distribution of standard updates to lower levels

review of system outputs

In licensing process

set up and maintenance of in –licensed /shared projects

Functional Expertize required for all the above areas

Scope of a Metadata registry for Medical Standards

Supports development projects in their entire lifecycle and all the associated workflows from protocol design to CSR and Submission

Enables documentation of justifications for adaptations and changes or their rejection

Builds the “backbone” of a future environment for clinical data

Supports flexibility to include cooperations with CRO’s, co-development, in-licensing

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Conclusion

Global Medical Standards supported by maintenance from a Metadata Registry with interlinked objects ,consumable to executing systems, will enable future efficiency gains in Pharmaceutical Development (and beyond)

Metadata registry maintained standards will provide a framework for reliable processes and output to internal and external customers of clinical data increasing internal agility and compliance to regulatory requirements.

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Thank you!