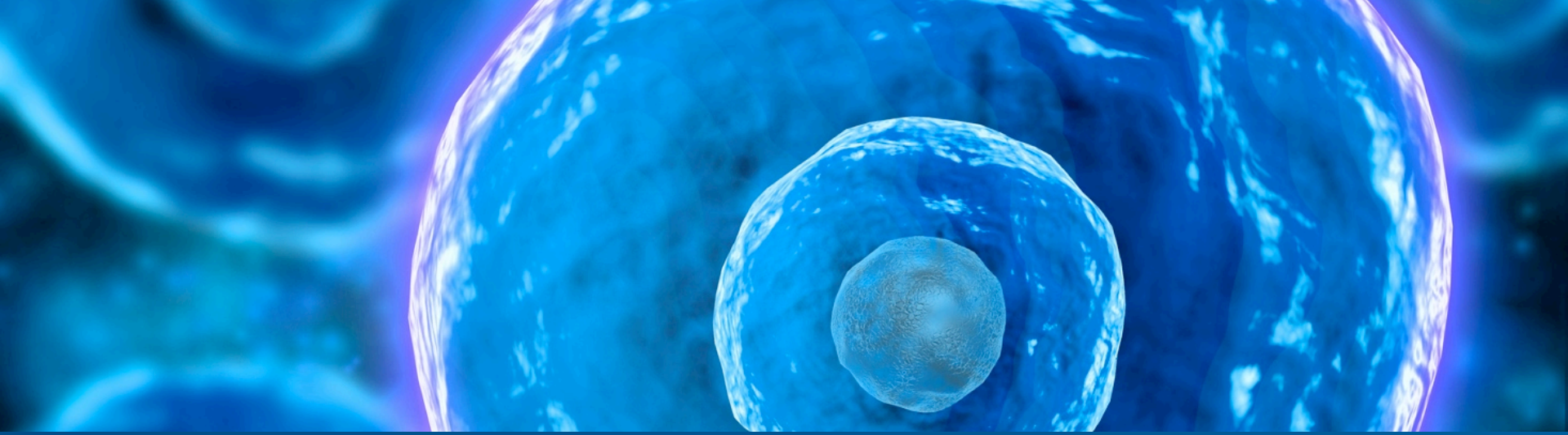

Phase 2 Platform trials more efficient and patient centric

Janssen Pharmaceutical Companies of Johnson & Johnson

Michèle Neeter, Data management Leader| Janssen Pharmaceuticals NV, Belgium| 11 Sep 2019

Group of human B-cells

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Platform HepB core team

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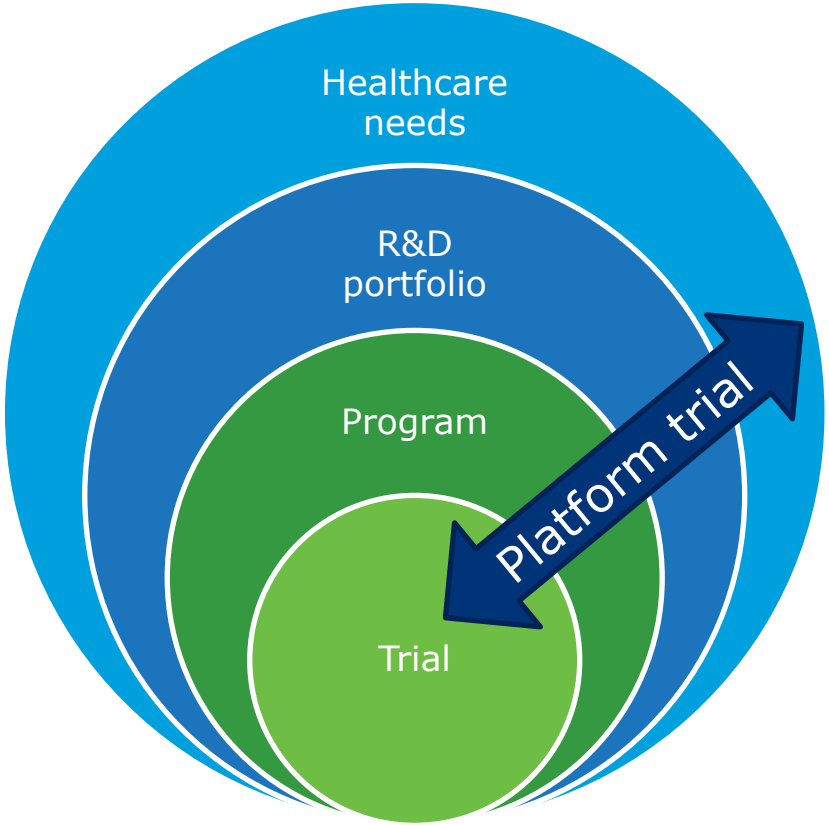
[1]Janssen Pharmaceuticals NV, Belgium, [2]Janssen Pharmaceuticals Inc, US, [3]Janssen Biopharma Inc., US, [4]Janssen Cilag France

Agenda

- Platform trial
- Value Proposition
- Data Standards and Data life Cycle Plan
- Conclusion

Platform trials

Transformational efficiencies to benefit patients



Shift from
***trial and compound centric* perspective**
to
***disease and patient centric* perspective**

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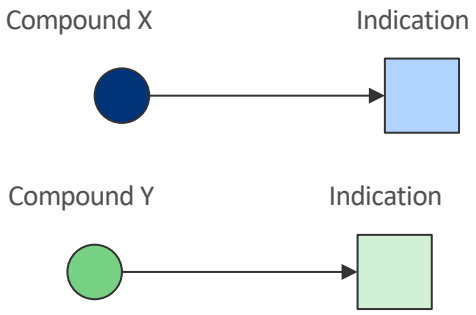
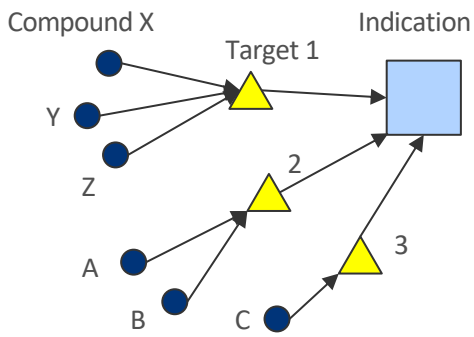
Separate studies versus platform studies

Base Case



Traditional clinical trial:
Study *one compound* against *one indication* at a time

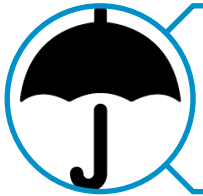
More Efficiency



Platform trials:
Efficiently study multiple compounds, potentially multiple targets in one operational set-up

Types of master protocols

Umbrella



To study multiple targeted therapies in the context of a single disease

	Drug 1	Drug 2	Drug 3	•••	Drug N
Type A					

Woodcock and LaVange, NEJM 2017

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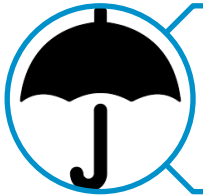
Types of master protocols

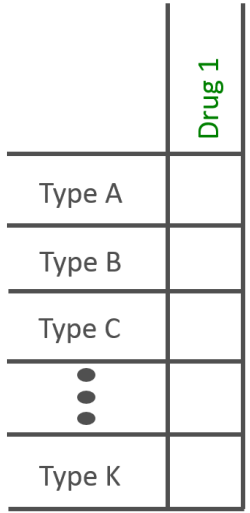
Umbrella



To study multiple targeted therapies in the context of a single disease

Basket

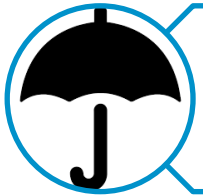
To study a single targeted therapy in the context of multiple diseases or disease subtypes



Woodcock and LaVange, NEJM 2017

Types of master protocols

Umbrella



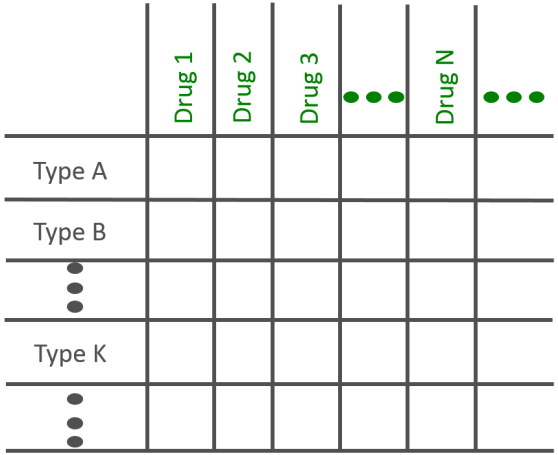
To study multiple targeted therapies in the context of a single disease

Basket

To study a single targeted therapy in the context of multiple diseases or disease subtypes

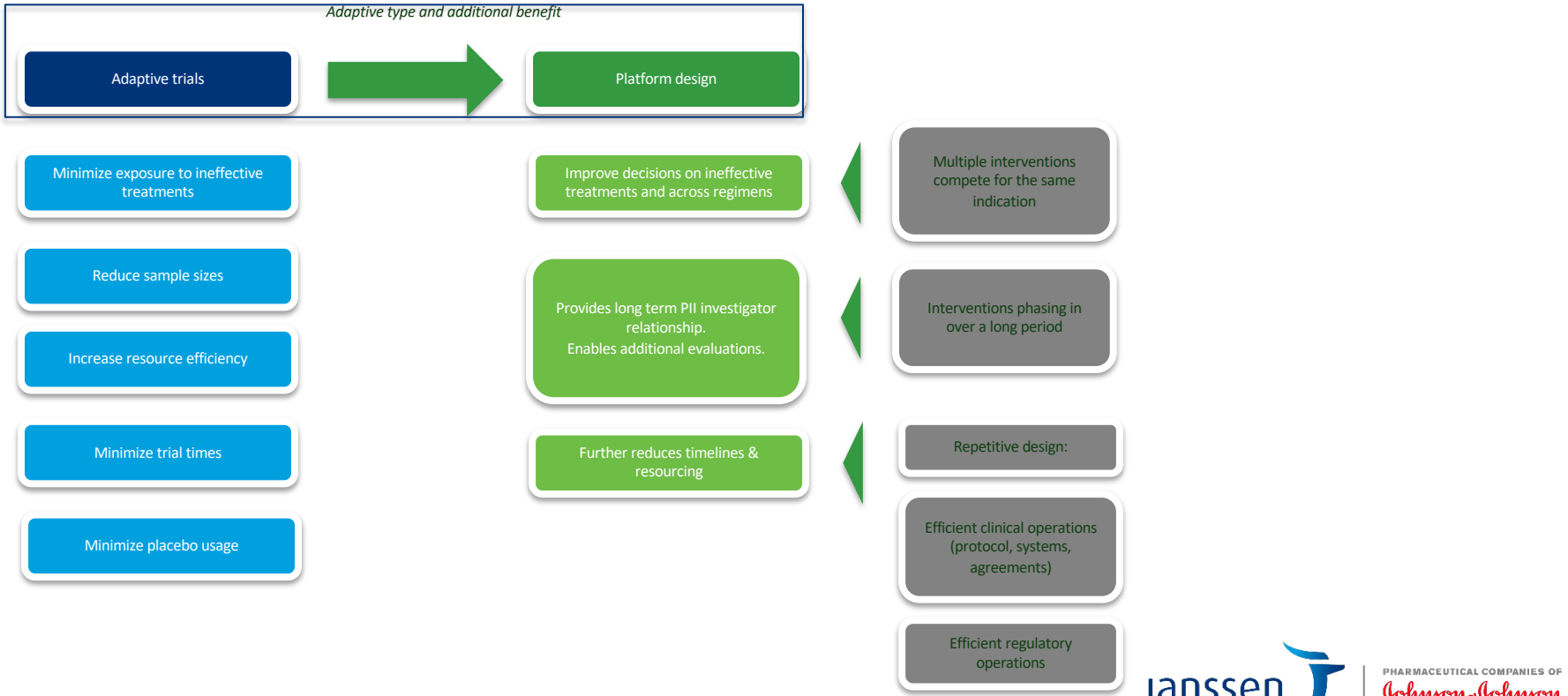
Platform

To study multiple targeted therapies in the context of a single disease in a perpetual manner, with therapies allowed to enter or leave the platform on the basis of a decision algorithm



Woodcock and LaVange, NEJM 2017

Additional benefits of platform design on top of benefits of adaptive trials in general



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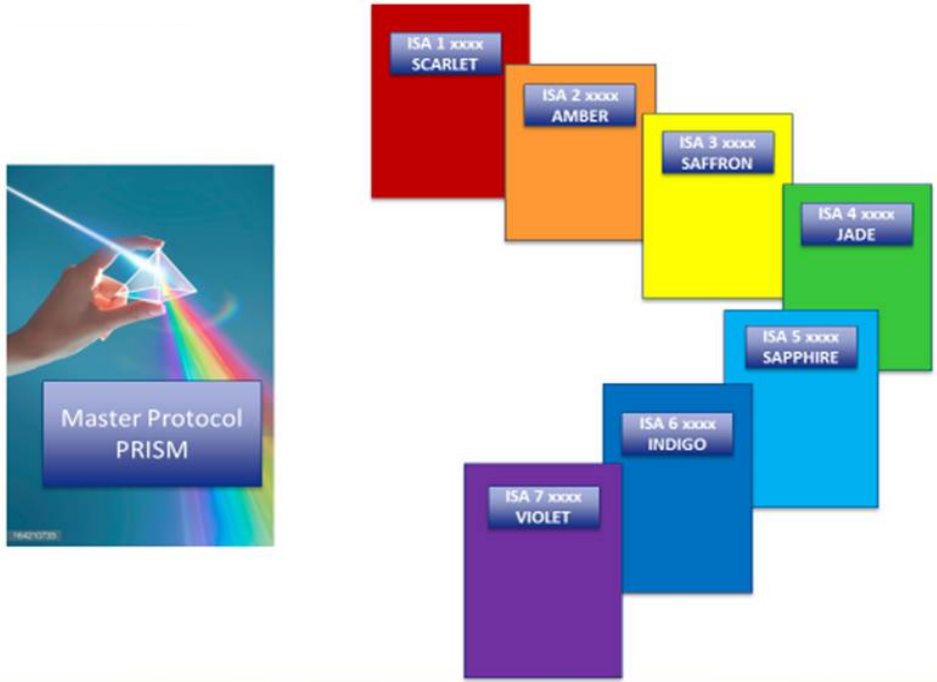
Master protocols to study multiple interventions

PRISM, a Janssen platform study in Crohn's Disease

In a platform trial, a **Master Protocol governs the entire study**, which includes the key study design elements

Drug specific data are provided in **Intervention-specific Appendices (ISAs)** which are added as new interventions/compounds enter the trial



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Hepatitis B Platform

Seahawk
Magpie
Osprey
Sandpiper
Warbler
Sparrow
Swan
Flamingo

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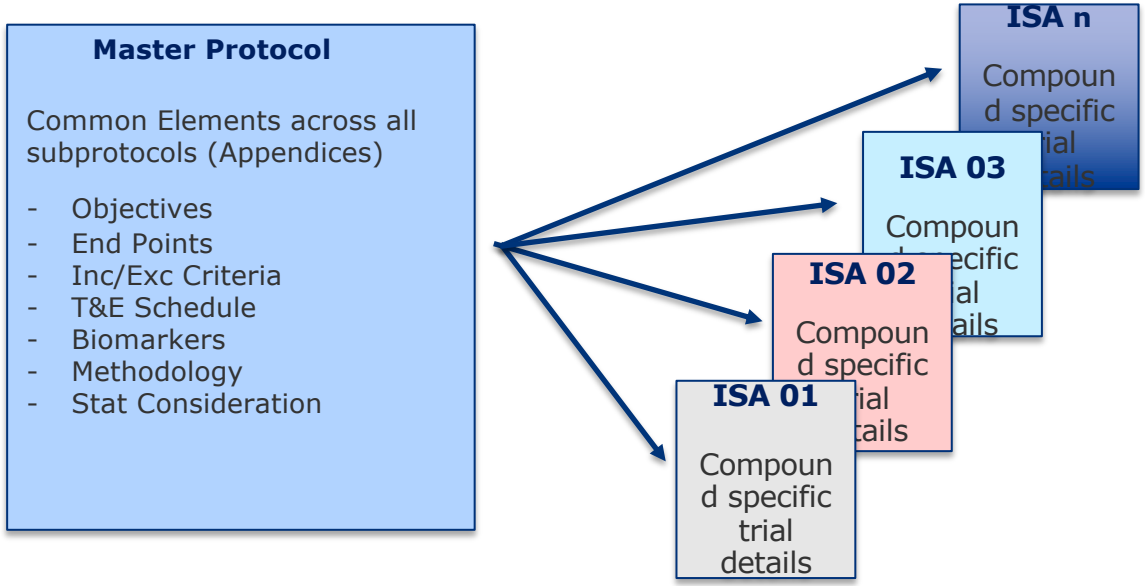
Multiple Trial Designs & Execution on One Platform



Execute within same operational infrastructure - Consistency, Efficiency and Quality Data

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Value Proposition

Value proposition

Benefit to patients

Inferential gains

Operational gains

Timeline gains

Cost efficiencies

Value proposition

Benefit to patients

- Best chance to access new, appropriate treatment options being evaluated
- Decreasing placebo/SoC arm size
- Options following screen failure or treatment no-response

Inferential gains

Operational gains

Timeline gains

Cost efficiencies

Value proposition

Benefit to patients

Inferential gains

- Improved power / smaller sample size
- Decision confidence comparing compounds
- Quality data from experienced, stable network of sites

Operational gains

Timeline gains

Cost efficiencies

Value proposition

Benefit to patients

Inferential gains

Operational gains

- Early engagement with sites (strategy; drafts)
- Long-term commitment together; pipeline of clinical trial work supporting investments
- Contracts: potential to leverage following first contracting ("platform contract")

Timeline gains

Cost efficiencies

Value proposition

Benefit to patients

Inferential gains

Operational gains

Timeline gains

- Easier to invest upfront for 1st ISA due to long-term view
- Acceleration following platform set up from operational efficiencies

Cost efficiencies

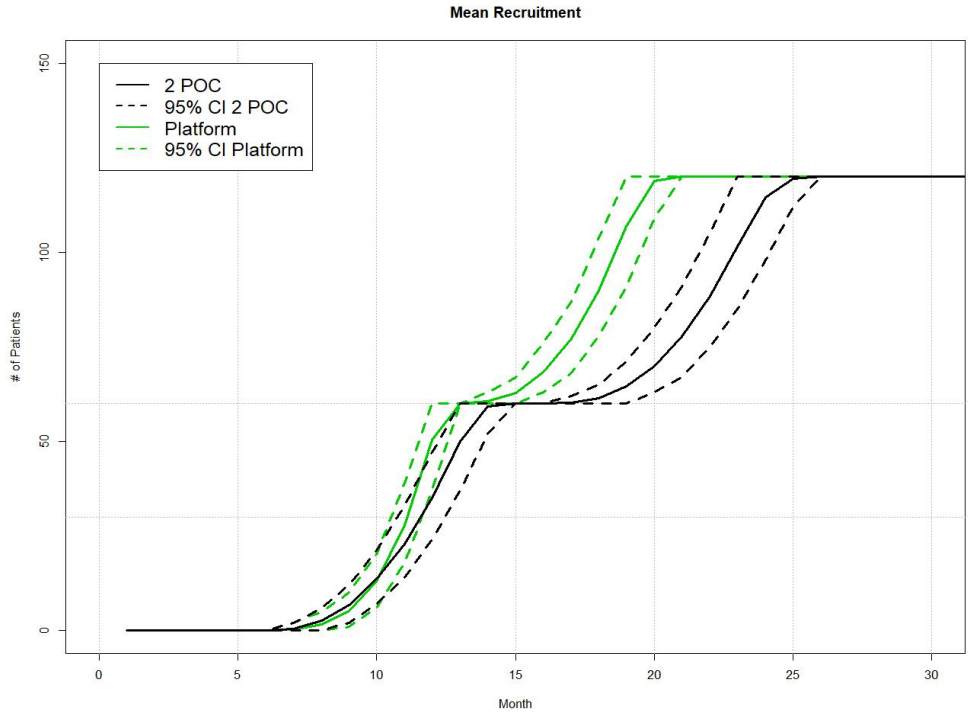
- Decision needed to investment up-front; efficiencies accrue over time

Specific Benefits for Enabling HBV Trial Platform

Platform	Benefits	HBV
Multiple MOAs	**Operational Efficiency Gained** *- contracting* *- same tools and training* *- reduced screen failure rate*	✓
Single Disease *- common I/E criteria* *- common primary endpoints* *- common biomarkers*	**Improved Decision Making** *- data consistency and high quality* *- (shared control/increased power)* *- (cross-ISAs comparison)*	✓
Perpetual Manner *- studied sequentially/parallel* *- new ISAs added as NMEs become available*	**Timeline Shortened** *- reproducible operations* *- large number of sites* *- reduced "ramp-up" time for new interventions*	✓

Timeline Gains in a Platform Study

Simulation of recruitment



Compared to 2 consecutive POC Ph2a studies, in a platform:

- First ISA may ramp up slower but can overtake due to higher enrollment as more sites are open
- Second ISA starts faster and recruits faster

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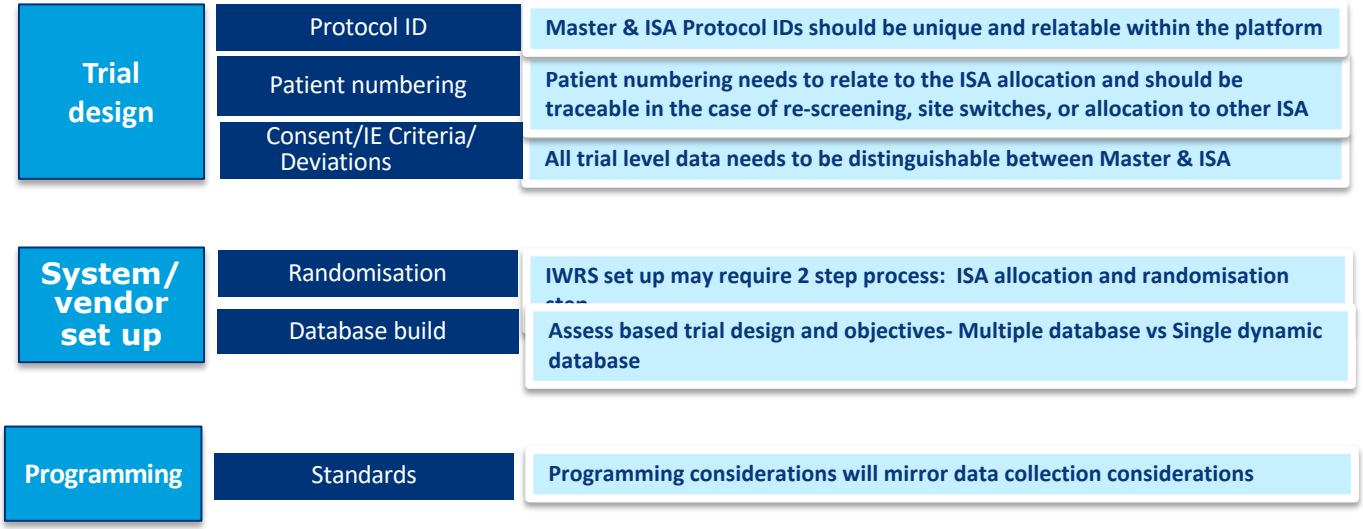
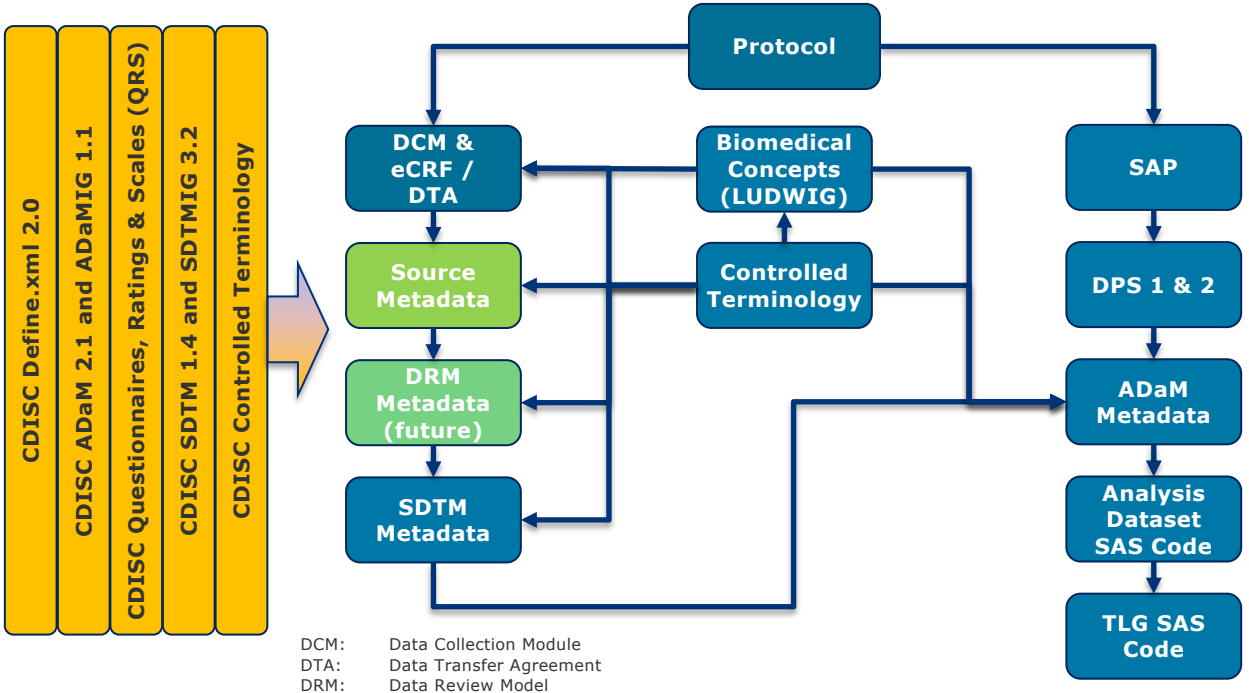
Standards & Data Life cycle Plan

Key considerations, IDAR Data Management



End-to-End (E2E) Standards



DCM: Data Collection Module
DTA: Data Transfer Agreement
DRM: Data Review Model
LUDWIG: Lab and Unit Dictionary Working and Implementation Group
SAP: Statistical Analysis Plan
DPS: Data Presentation Specifications
TLG: Tables, Listings and Graphs

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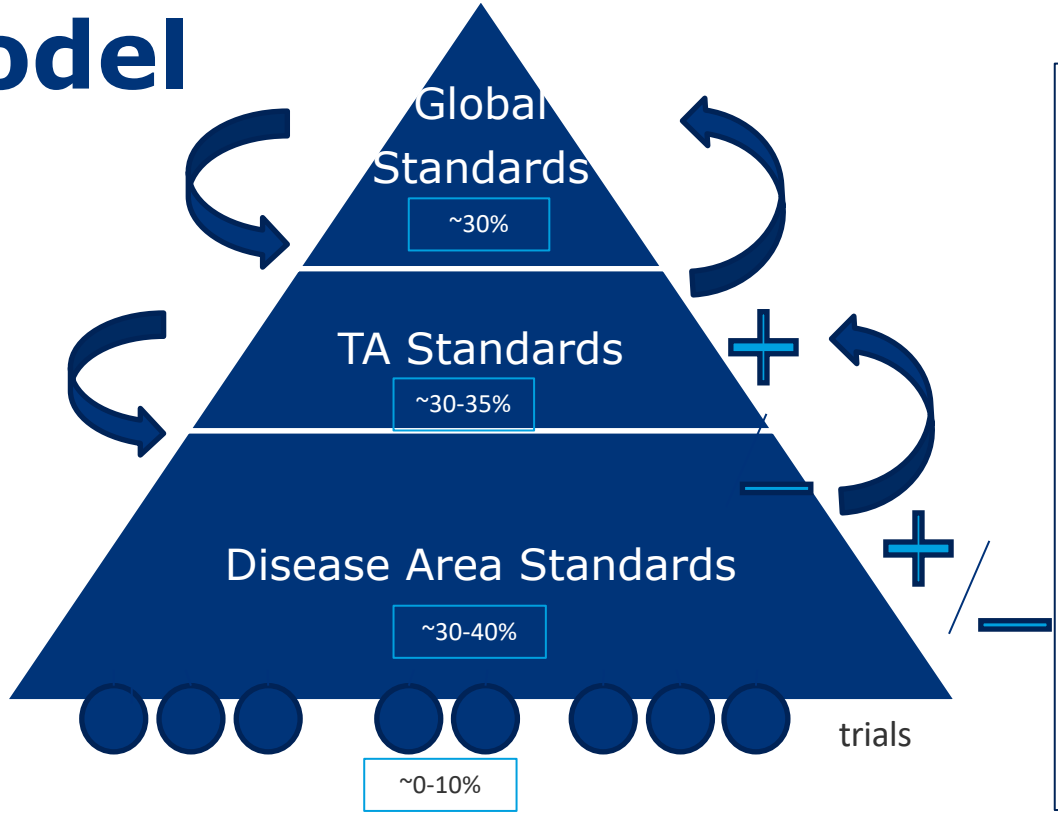
New Standards Development Model



- Our new proposed governance model focuses on inheriting and promoting standards from the Trial → Disease Area → TA Standards → Global Standards.
- Trials are used to build the Data Life Cycle Plan (DLP) for Disease Areas.
- If two disease areas have consistent standard elements, these elements are promoted to TA Standards
- If two TAs have consistency, those standard elements are moved to Global
- This model works backwards as well, as disease area inherit standards from global, etc.

What is a Data Life Cycle Plan (DLP)?

DLP is a framework for end-to-end standards content

- Utilize standards tailored to the needs of a specific Disease Area.
- Pre-selection of options in Global Topics (DM, AE, LB, ….) for Disease Area
- Specific content for efficacy, disease-specific safety, PRO/COA, …

Data Life Cycle Plan

What do we standardize?

- Start with standard tables, listings, and figures (TLF) mock-ups: DPS Part 1
  - Select options for Disease Area
- Review available standard CRFs (TA preconfigured or global) and identify design considerations for DA needs (if necessary)
- Update statistical requirements: SAP, DPS Part 1, and DPS Part 2

Data Lyfe Cycle Plan

What do we standardize? (continued)

- Update CRFs, edit checks and completion guidelines.
- Update the technical specifications / systems required to enable end to end standards, e.g. mapping to SDTM
- For New Standards:
  - DLP team promotes trial level content to Disease Area standard following above steps
- TA Governance Council oversight of above

What's the benefit of DLP?

- **End-to-End Disease Area standards from:**
  - Applying the options in the "Global" standards (DM, AE, LB, CM, etc.) to the DA specific needs across trials.
  - Building the DA topics (Baseline Disease Characteristics, Efficacy, etc.) to work across trials.
- **Reduced cycle times**
  - Reduce time in study setup
  - Reduce time to database ready/data available
  - Reduce time to topline and routine analysis
  - Reduce time to scientific exploration
- **Quality by design**
  - Increase quality of data collected
  - Predictable data collection and reporting methods, agreed cross-functionally
- **Compliance with regulatory expectations**
- **Efficiencies in clinical development trial processes through high level of reusability**

DLP Process

- **Define scope – what topics will be covered**
  - Prioritize topics and organize in logical groupings → workshops
- **Within individual workshops, review content by topic**
  - Review existing standard content in the Global topics. Document decisions:
    - What content to keep?
    - What content to drop?
    - What choices are study-specific?
    - Provide rationale for decisions or further guidance
  - Review decisions
    - Internal Work Group review
    - Extended team review
  - Promote trial level analyses to DA level where applicable
- **Finalize and sign off by topic**
- **Build preconfigured standards based on existing standards/ trial-level content**
  - Starting with available standards and tailor to Hepatitis B needs
  - Review and sign off on preconfigured standards
  - Will be used to build standard SDTM/ADaM metadata and SAS code (if applicable)

Conclusion

- Paradigm shift from a compound focus to portfolio thinking
- Patient centric perspective
- Creating inferential and operational efficiencies
- End to end Disease area Standardization
- Reduced cycle times and reusability
- Quality by Design

THANK YOU

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