

PP23 Integrated clinical databases to detect safety signals across products and indications

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Objective

To create integrated databases (AdVac) cross studies and indications to speed up the process of identifying recurring safety issues, especially the rare signals.

Introduction

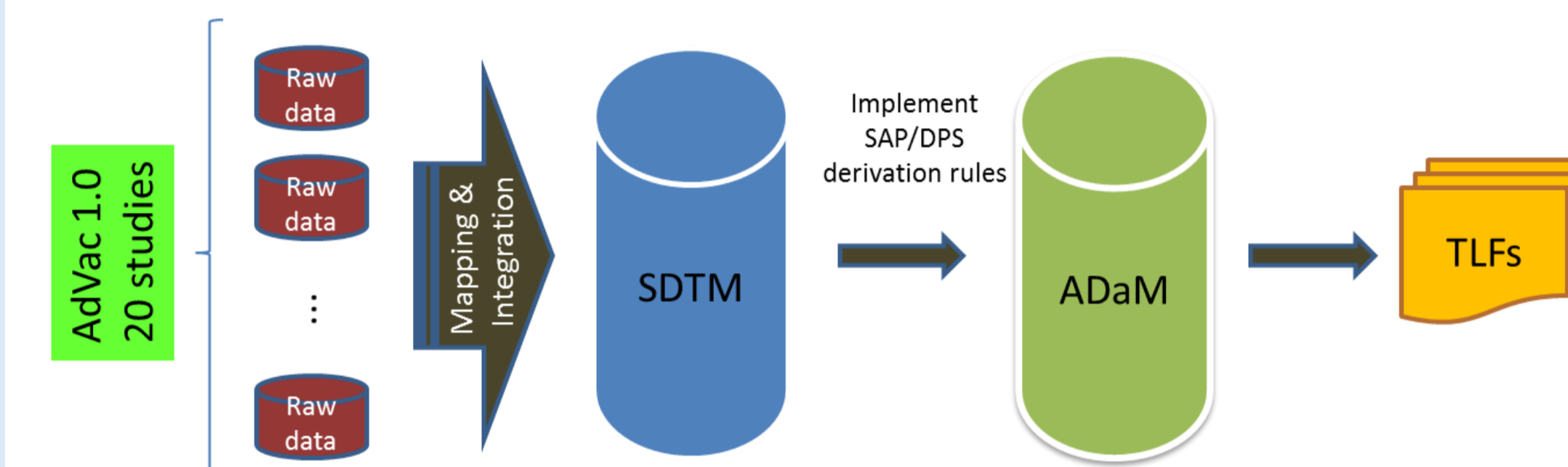
- ❖ The use of adenoviruses (Ad) as vaccine vectors against a variety of pathogens has demonstrated their capacity to elicit strong antibody and cell-mediated immune responses cross indications
- ❖ Our company has a broad spectrum of vaccine portfolio using Ad as a vector.
- ❖ In order to increase robustness of signal detection cross studies and indications, a data pooling model is created.
- ❖ In this pooling model, all clinical data are mapped to SDTM domains and only selected data which are used in AdVac Safety Report are converted to ADaM datasets.
- ❖ The ADaM database is used to detect anticipated safety signal, while SDTM for Ad hoc signal detection.
- ❖ We update the integrated Adeno-based Vaccine (AdVac) databases including both SDTM and ADaM on an annual basis.
- ❖ The annual AdVac Report, a submission document which is similar to Investigational brochure, is published at the end of each year.

Data Flow Models

For efficiency purposes, a stage hybrid data pooling model is utilized to create the AdVac databases.

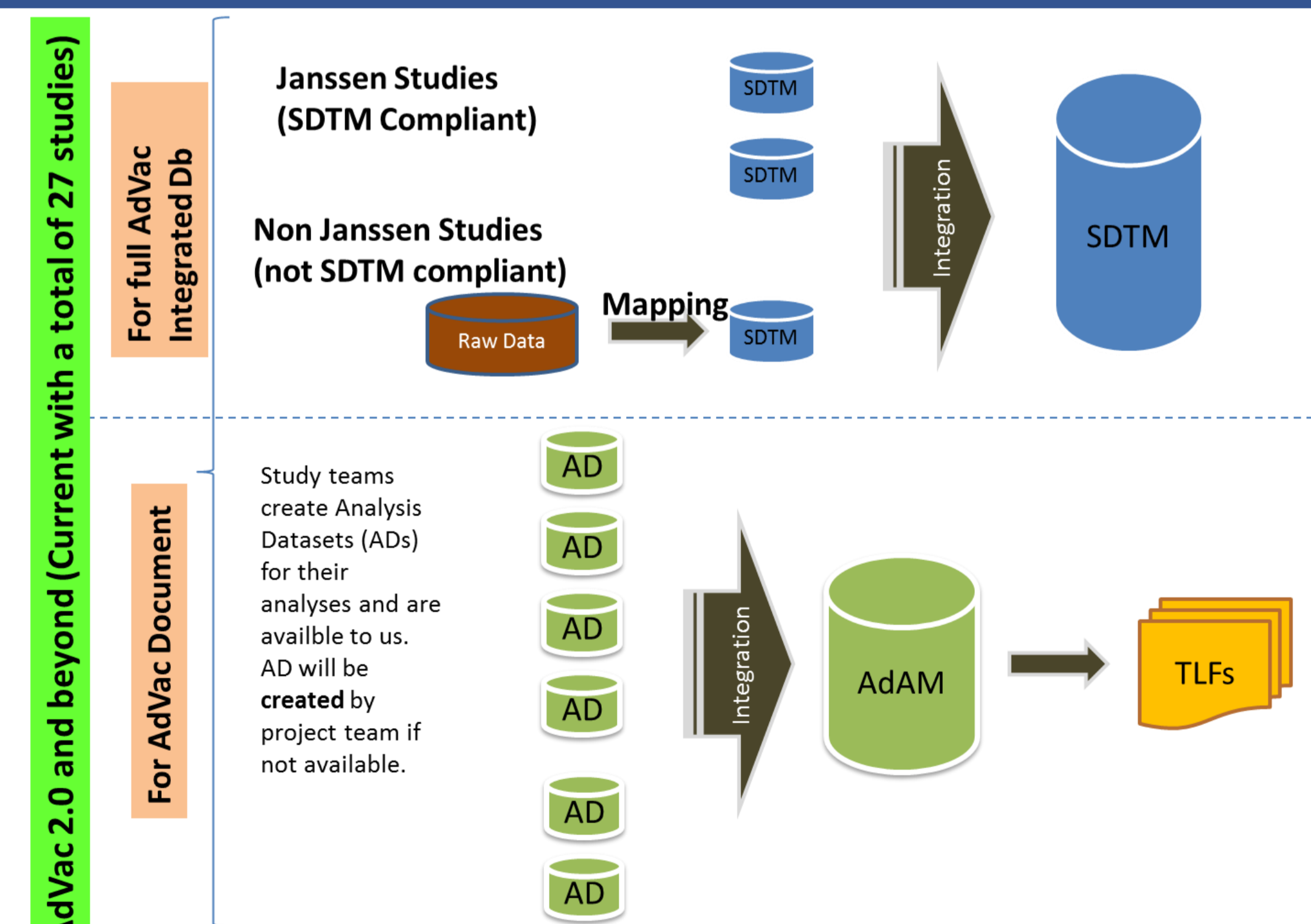
Data Flow in Stage I

- ❖ 20 legacy clinical studies from different partners (they were in different data structures and not SDTM compliant)
- ❖ First, a harmonized SDTM AdVac database was created.
- ❖ The SDTM domains related to solicited and non-solicited AEs, DM, EX were converted to ADaM Database. No study specific ADaM Databases were generated.
- ❖ Tables, Listings and Figures (TLFs) were created from ADaM
- ❖ Pro: an efficient process – One ADaM instead of 20 ADaM databases was generated
- ❖ Con: No trial specific rules can be applied



Data Flow in Stage II

- ❖ The AdVac ADaM Database including selected domains (AE, CM, SR, FA, VS, LB, DM, DS) is updated from individual study ADaM Datasets.
- ❖ This database is used to create the TLFs and the AdVac Report.
- ❖ In addition, a pooled AdVac SDTM database is created to include all domains (35 domains & 19 SUPP domains). This database is used for any Ad hoc questions and acts as the source for data mining.
- ❖ Pro: efficiency & data accuracy
- ❖ Con: different study specific rules may be applied so homogeneity may be an issue.

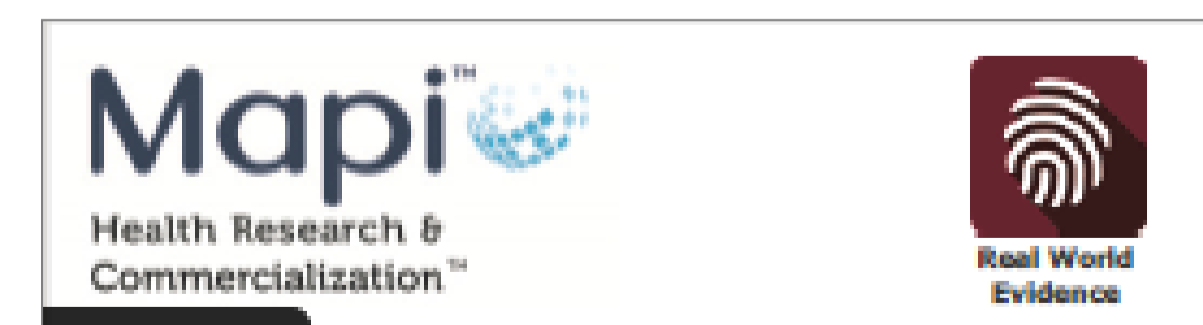


AdVac Program

Indication	Vaccine	Partner
Malaria	rAd35.CS and rAd26.CS prime boost rAd35.CS and RTS,S prime boost	Novartis, GSK
TB	rAd35.TBS (boost to BCG)	AERAS
HIV	rAd26 prime boost + protein rAd26 and pox prime boost + protein	Novartis, GSK, Merck, Janssen
Ebola	rAd26 and pox prime boost	Novartis, GSK, Merck, Janssen
RSV	rAd26 prime boost rAd35 and rAd26 prime boost	Janssen
HPV	rAd35 and rAd26 prime boost	Janssen
Herpes zoster	Adenovector prime boost	Janssen

Challenges

- ❖ SDTM pooling:
 - The biggest challenge was integrating and homogenize the study databases which are non-SDTM compliant. They came from different providers and greatly differ from one other.
 - Different mappings and different versions of SDTM may be used by each study.
- ❖ Analysis Dataset pooling
 - Different studies potentially use a different ADaM model, requiring harmonization with respect to variable names and content
 - Meaningful pooling is more than a technical process (decisions are needed regarding what to do with products we are not interested in, open label studies, co-administered products...)
- ❖ Disconnect between AdVac SDTM and AdVac ADaM databases



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