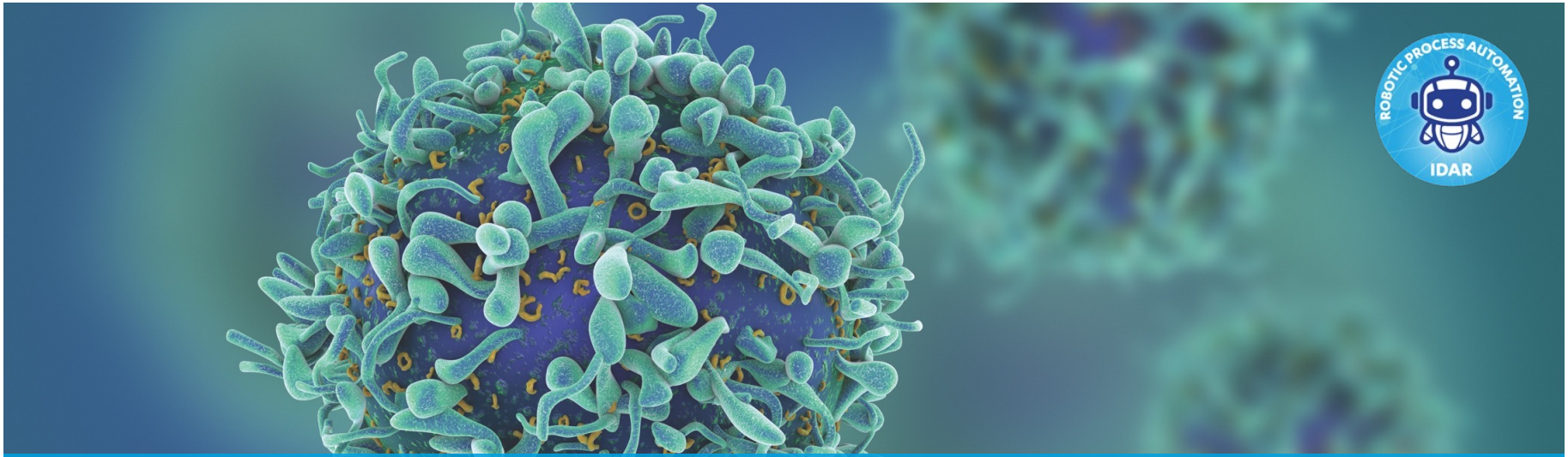

Automated checks and delivery of submission-ready packages using Robotic Process Automation (RPA) BOTs.

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3D illustration of T cells or cancer cells

PHUSE SDE, Zurich
September 2023

janssen | PHARMACEUTICAL COMPANIES OF Johnson & Johnson

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Background

- Study data included in electronic submissions must be in a **format that a Regulatory Health Authority (RHA) can process, review, and archive**.
- An **RHA may refuse to accept an electronic submission package**, if the study data format is not submission compliant.
- Data intended for a submission to Regulatory Health Authorities must:
  - be **compliant** with the submission requirements
  - undergo a **QC process**
  - be delivered to the Submission Publisher in the **appropriate format/structure**
- **RHA release requirements and Sponsors implement**.

Janssen Implementation

- Janssen has developed a series of guidance and tools supporting processes related to creating submission-ready documentation to support clinical data submissions.
- It includes a suite of tools that is **using Robotic Process Automation (RPA) BOTs** :
  - **automated checks** on submission packages
  - **automated delivery of the said package** to the internal electronic publishing output network drive in accordance with **Electronic Common Technical Document (eCTD) folder structure** needed for publishing

What are RPA BOTs ?

RPA: Robotic Process Automation

BOT: short for roBOT

Digital Workforce

Interact with any system or application the same way a human worker would

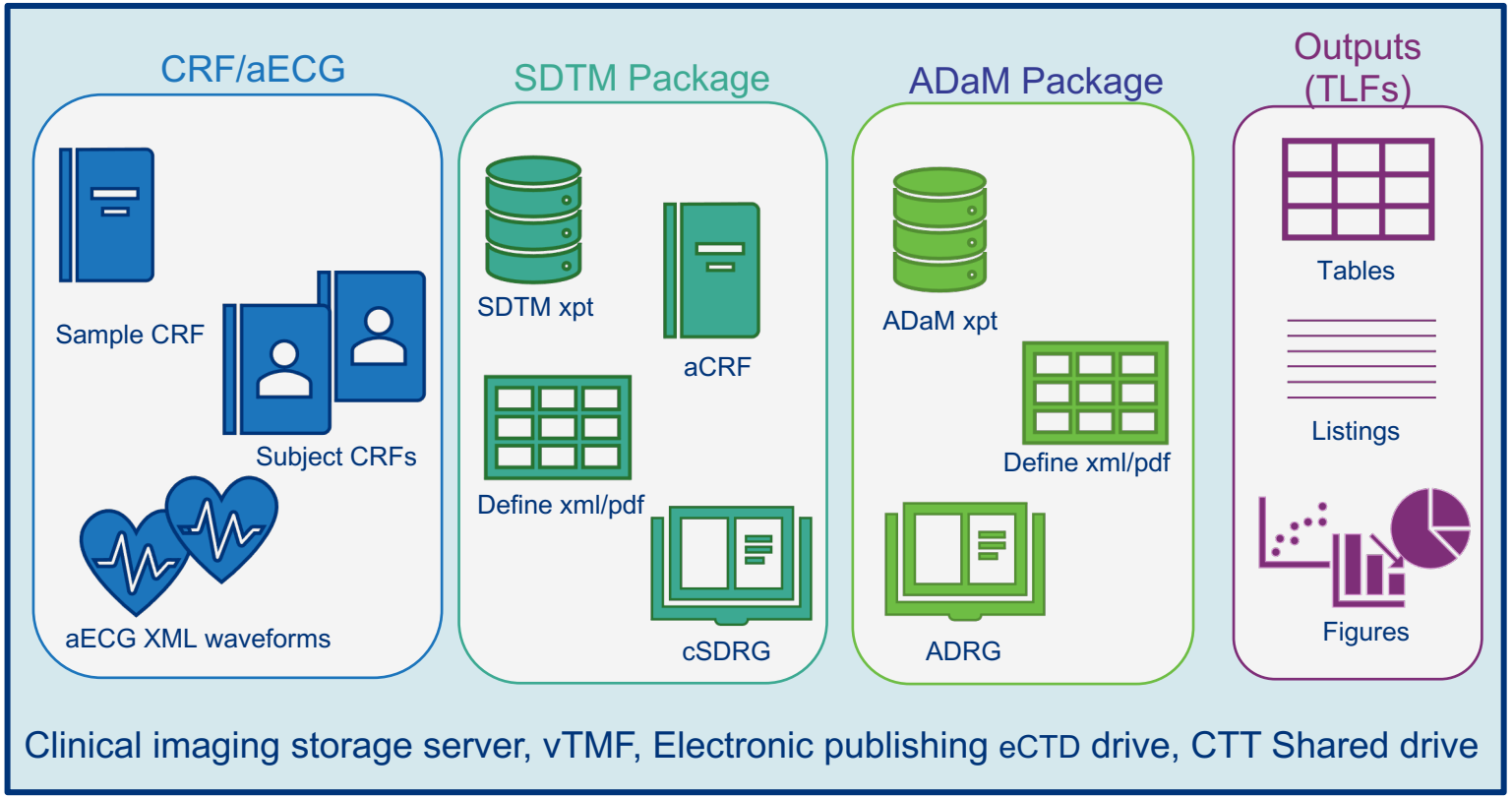
AUTOMATE certains tasks without specific instructions from human

Scope

CHECK
Ongoing
&
Final

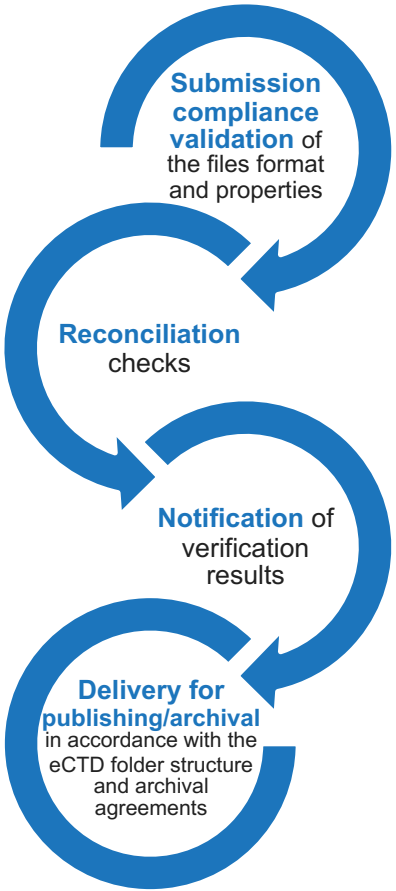
SEND NOTIFICATION
verification results

DELIVER
Final



TMF= Trial Master File
CTT= Clinical Trial Team

eCRF & aECG RPA BOT



- Subject CRFs in PDF
- Annotated ECG Waveform files (aECG XML files)
- Sample CRF

- Subject CRF(s) vs narrative list
- aECG XML Files vs EG.xpt
- Current aECG XML submission package vs previously submitted aECG XML package

- Overall status (success, fail, rejection)
- Summary of issues with severity and recommendations for resolution
- Attachment with detailed validation report (xls)

- Subject CRF(s) and aECG XML files to Electronic publishing eCTD drive
- aECG XML files to the Clinical Imaging storage server
- Sample CRF to vTMF

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- **All files are checked** (as opposed to manual QC where only a sample was checked) => Minimized manual work and human error
- **Resolution recommendations** provided for identified issues

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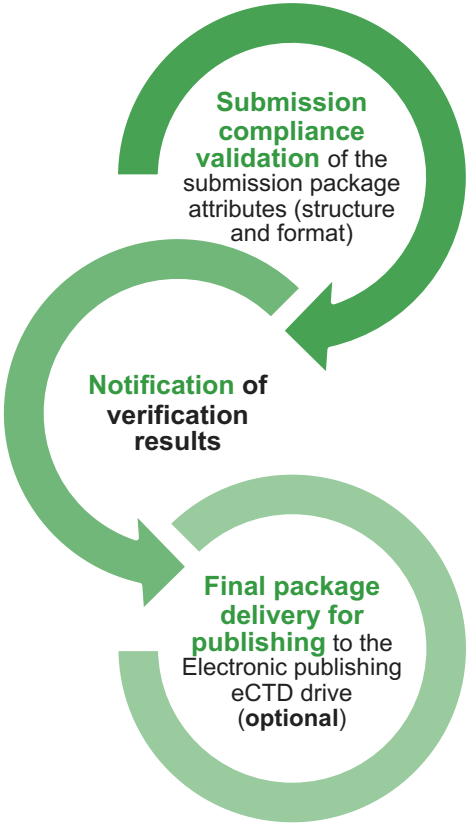
- **Cannot be used for legacy** or paper-based studies (RAVE CRF only)

SDTM and ADaM e-Submission RPA BOTs



- Checks presence of required files, file type, naming conventions, files size, folder structure, attributes and content of define.xml, define.pdf, cSDRG, ADRG, aCRF…

- Overall status (success, fail, rejection)
- Summary of issues with severity and guidance for resolution
- Attachment with detailed validation report (xls)

- Submission package delivered to electronic publishing eCTD drive, with email confirmation and report

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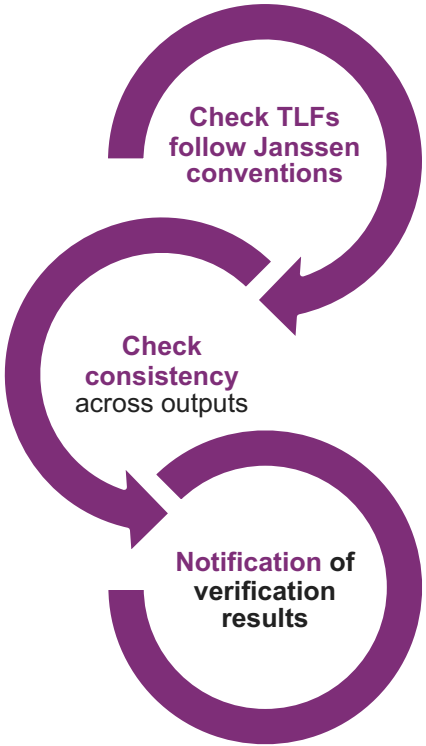
- Ensure PDF documents within a package meet the attribute requirements as described in the **FDA's PORTABLE DOCUMENT FORMAT (PDF) SPECIFICATIONS** in alignment with ICH M2 recommendations
- Ensure documents are in a **format that the receiving center for submission, CDER or CBER, currently supports**
- Ensure submission package is present in the **correct folder structure (in accordance with the (eCTD) folder structure)**

–

- **Cannot be used for legacy** or paper-based studies
- **Does not fully check hyperlinks** in define.xml/pdf: check bookmarks are valid (not broken), collapsed…that but not that they point to intended location

TLFs Consistency BOT



- Checks font, letter cases, file names, mandatory content etc.
- Checks file size does not exceed 20kb

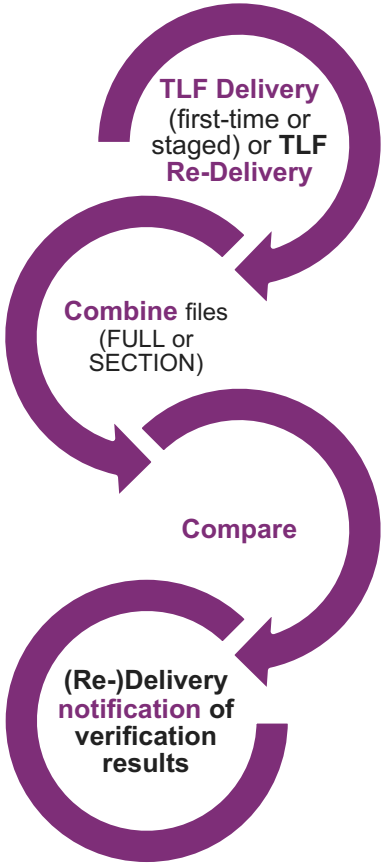
- Compare population rows
- Cross-check tables
- Consistency between titles file and rtf files

Summary email sent with:
- Consistency check outcomes
- Report detailing failed checks

- Can be used for both **in-house and outsourced trials** (following Janssen process, and using standard reporting macros)
- Only titles file and .rtf outputs required
- **Issues identified early**, reducing volume of changes required after cross-functional reviews
- Can be **run by any assigned team member**, not lead programmer only

- Only for use with **outputs created in standard way**

TLFs delivery and re-delivery BOT



- Copy TLFs identified for the request to the TLF delivery location
- Generate TOC_yyyymmdd.xml
- For redelivery, create Obsolete (CSR not published) or errata_corrected (CSR published) subfolder

- Combine TLFs identified for delivery from the TLF delivery location into 1-n combined bookmarked pdf file(s)
- Automatically generates bookmarks

- Compare folder contents (TLF presence & timestamp) of the TLF package location with folder contents of the TLF delivery location

Generate TLF BOT report email with :
- BOT outcome report
- Compare report

Generate TLF (re)delivery notification email upon successful (re)delivery

- **Combine only** and **compare only** modes available
- Can be used even if CSR is already published
- **TLF (re)delivery notification** sent to stakeholders

- Limited to **TLFs in production or preproduction** in Janssen statistical computing environment
- Compares only file names and date/timestamps; **file contents are not compared**

What our RPA BOTs do not do

BOT **does not manipulate** the content of the submission files.

BOT **does not replace any established Standard Operating Procedures**.

BOT **does not replace Risk-Based Quality Review** of deliverables

BOT **does not replace any compliance validations** (e.g. Pinnacle 21, Janssen proprietary checks) performed on study data/metadata during trial conduct.

BOT does not check ALL submission package attributes:

some checks cannot be programmed

=> **QC Checklists**

Step n°	Step details	Result: Manual Verification	Result: SCnDT RPA BOT Validation	Comment
1	Check whether the naming of the zip file: • Submission-ready SDTM package has the following format: 'DBR_UNIQUE_RELEASE_NAME_YYYYMMDD_TRIAL NAME_SUBXXX' (where XXX indicates the CDISC SDTM implementation guide version that was followed, and YYYYMMDD is the date the entire database was declared not subject to change, this is the date the latest database lock notification was sent for the data being submitted (i.e., for staged releases, the date of the latest database lock notification)). e.g., DBR_FL_YYYYMMDD_BESTTRIALNOW1001_SUB32 • For the Legacy packages: ''DBR_UNIQUE_RELEASE_NAME_YYYYMMDD_TRIAL NAME_LEGACY''**	☐ OK ☐ Not OK, please add a comment	☐ OK ☐ Not OK, please add a comment	
2	Check whether the following files are present in the submission-ready SDTM package: • SAS version 5 transport files (.xpt files) • define.xml and associated define.xsl* • define.pdf • acrf.pdf (Annotated Case Report Form) • csdrg.pdf (Clinical Study Data Reviewers Guide (cSDRG)) *define.css and icon.gif files could be included in a SDTM package when define.xml v1.0.0 was utilized.	☐ OK ☐ Legacy n/a ☐ Not OK, please add a comment	Not applicable*	

Benefits of our RPA BOTs

Extensive Automated Verifications of file formatting and file structures of **ALL** submitted files – both during trial conduct and final stage.

As a result, **increased quality confidence**.

Automated Validation for Submission Compliance: for issues identified during the validation, a report will be generated and sent to the validation requester.

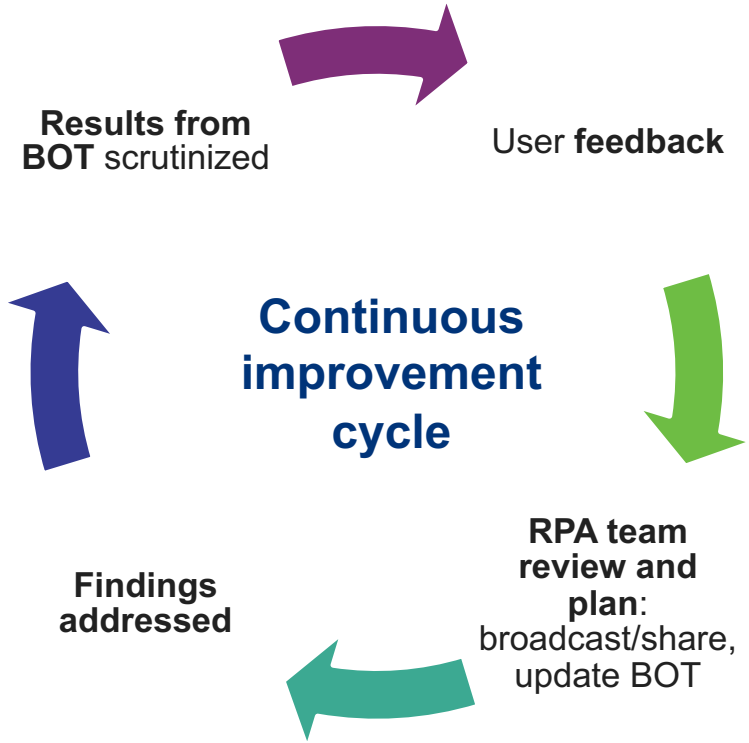
Assurance that the submission preparation process was followed **consistently**. Minimal chance of getting questions from HA on these deliverables during the submission review, that can result in a potential delay in drug approval.

Automated folder structure creation and delivery to the publisher or archival (when passes validation).

Time reduction for verification and delivery of these files: manual work reduction, faster overall QC/delivery time, human error reduction.

RPA BOT Support and Maintenance

- **RPA team**: tech support, SMEs
- **Guidance documents**: SOPs, Job aids, checklists, guidance on interpretation of validation results
- Virtual business support **help desk**
- Focused training, experience sharing and **Q&A** sessions




ROBOTIC PROCESS AUTOMATION
IDAR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