

DACHS

Reliable, competent,
and flexible IT services
in a strict regulatory
environment



How to Accelerate Your Submission Content Preparation

Lessons Learned including
MS Word Tips

2023-03-30

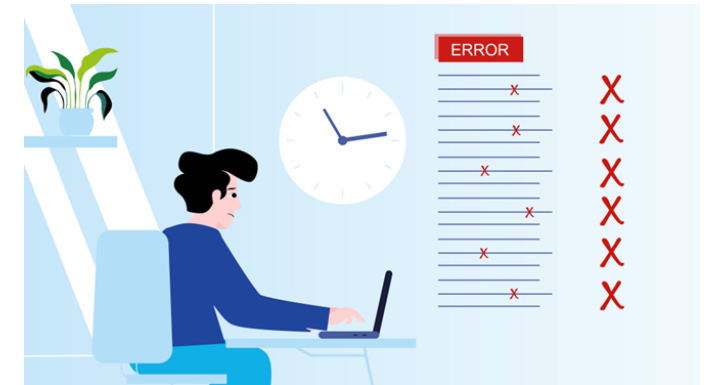
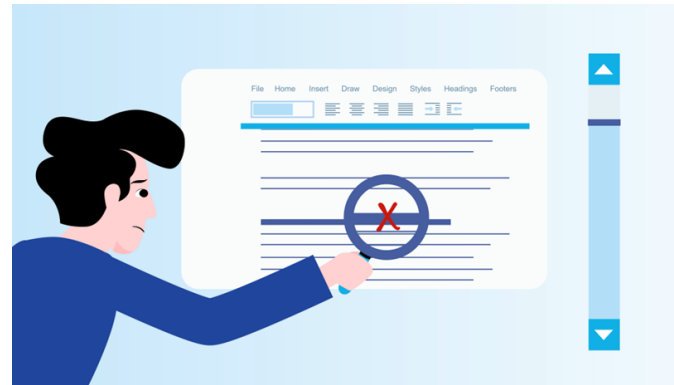
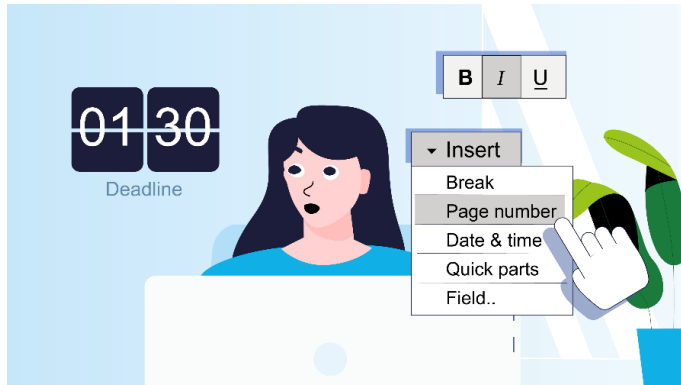
▶ Understand that:

- ▶ You can save a lot of time & reduce the risk of non-compliance
- ▶ Validation is possible much earlier in the submission process
- ▶ Many of your checks and fixes can be automated



▶ Typical Submission Content Preparation Workflow

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▶ Why?

- ▶ It is critical for successful submissions

▶ How do we reach technical compliance?

- ▶ Following industry standards and good authoring processes
- ▶ Creating compliant PDF from compliant source Word document
- ▶ With the correct tools the process can be simplified



9.4 Treatments

Headings include whitespaces

9.4.1 Treatments Administered

The precise treatments or [diagnostic agents](#) to be administered in each arm of the study.

Link issues

Figure 10-1 Drug Ω Development Process

Empty paragraphs

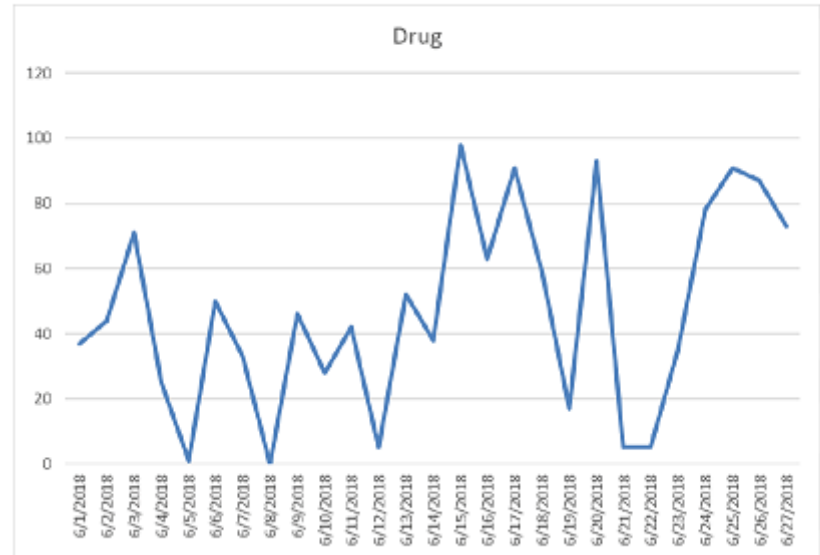


Image not in-line with text

Watermarks exist

9.4.2 Identity of Investigational Product(s)

In the text of the report, a brief description of the test drug(s)/investigational product(s) (formulation, strength, batch number(s)) should be given. If more than one batch of test drug/investigational product was used, patients receiving each batch should be identified in appendix 16.1.6.

[Figure 14-1](#)

Comments exist

9.1 Clinical laboratory evaluation

Out of sequence numbering

9.1.1 Listing of Individual Laboratory Measurements by Patient (16.2.8)

When required by regulatory authorities, the results of all safety-related laboratory tests should be available in tabular listings, using a display similar to the following.

Table not set to page width

Table 3 List of Laboratory Measurements

Patient	Time	Age	Sex	Race	Weight	Dose	SGOT	SGPT	AP...X
#1	T0	70	M	W	70 kg	400mg	V1*	V5	V9
	T1						V2	V6	V10
	T2						V3	V7	V11
	T3						V4	V8	V12
#2	T10	65	F	B	50 kg	300mg	V13	V16	V19
	T21						V14	V17	V20
	T32						V15	V18	V21

* Vn = value of a particular test

- ▶ Problems with Word documents can cause rendering problems
 - ▶ Use of not inline embedded objects/images
 - ▶ Incorrect margins or paper size
 - ▶ The presence of unused bookmarks in the source document
 - ▶ Inconsistent or improper use of styles
 - ▶ Corrupted style configuration/settings
 - ▶ Invalid/damaged fields; broken links or cross-references
 - ▶ Hidden/instructional text remaining in the source document
 - ▶ Revised text/comments not removed

▶ Regulatory guidance vs. typical PDF issues

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The screenshot shows a PDF viewer interface with a document titled "Test Document.pdf". The document content includes a header with the "DACHS" logo and a large "WATERMARK" text. Below the watermark, the document is titled "Clinical Development" and contains several sections of text, including "Title of Study", "Generic Name", "Name of Test Drug", "Indication Studied", "Name of the Sponsor", "Development Phase of Study", "Study Initiation Date", "Study Completion Date", "Name and Affiliation of principal or coordinating investigator(s)", "Practices", and "Date of the Report". At the bottom, it lists "Document type", "Document status", and "Release date".

Annotations and red boxes highlight the following issues:

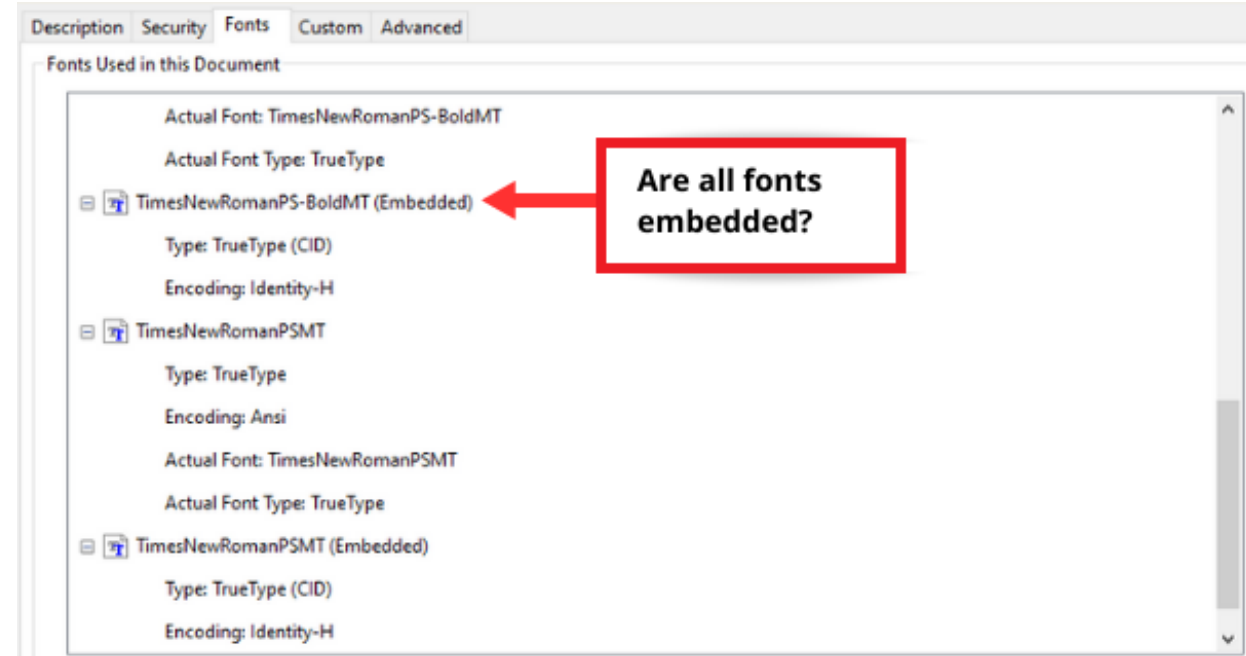
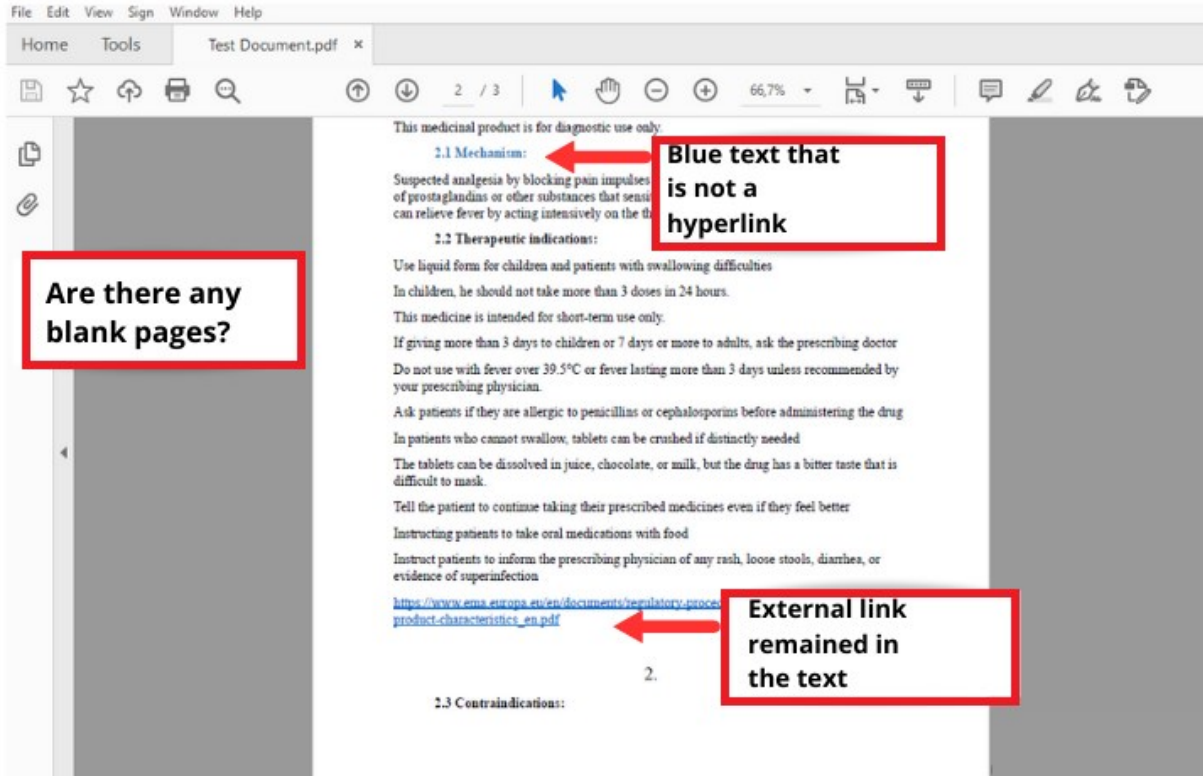
- Does the PDF open to page 1 or TOC?** (points to the page number "1 / 3")
- Is the first page orientation portrait?** (points to the page content)
- Is the PDF protected by open password?** (points to the document content)
- Does the first page and the headers indicate 'draft'?** (points to the "Document status: Draft" text)
- Are there any watermarks?** (points to the "WATERMARK" text)
- Does the PDF contain non-configurable annotations?** (points to the "WATERMARK" text)
- Is the page numbering continuous?** (points to the page number "1")

The screenshot shows the "Description" and "Advanced" tabs of a PDF properties dialog box. The "Description" tab shows fields for "File", "Title", "Author", "Subject", and "Keywords". The "Advanced" tab shows fields for "PDF Producer", "PDF Version", "Location", "File Size", "Pages", "Tagged PDF", "Number of Pages", and "Fast Web View".

Annotations and red boxes highlight the following issues:

- Are PDF properties specified?** (points to the "Title" field)
- Is the PDF version correct?** (points to the "PDF Version: 1.7 (Acrobat 8.x)" field)
- Is the PDF file size too large?** (points to the "File Size: 131,43 KB (134 585 Bytes)" field)
- Is the PDF optimized for fast web view?** (points to the "Fast Web View: No" field)

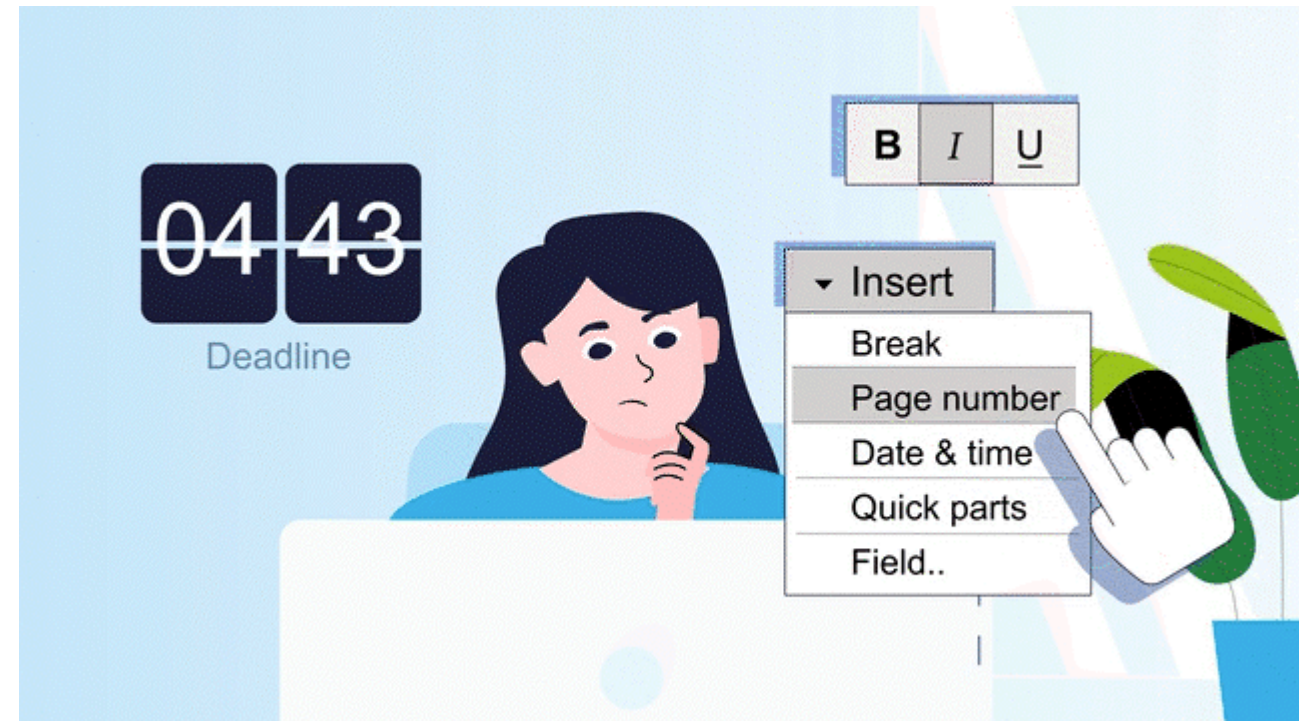
▶ Regulatory guidance vs. typical PDF issues



▶ Painful Formatting Challenges Authors Face

10

- ▶ Reformatting external, existing content
 - ▶ Using the correct template
 - ▶ Using correct list formats, figure numbering
 - ▶ Using correct table formats
 - ▶ Manual identification and fixing of issues
 - ▶ Slightly different requirements imposed by multiple health authorities
 - ▶ Repetitive tasks
 - ▶ Time-consuming, complicated processes
 - ▶ Multiple tools required
 - ▶ Risk of Refusal To File
 - ▶ Missed deadlines
-
- ▶ **Slow + Complex + Risky**
 - ▶ Where have YOU had the biggest issues?



- ▶ Poor-quality documents
- ▶ Manual identification and fixing of issues
- ▶ Repetitive issues and tasks
- ▶ Time-consuming, complicated processes
- ▶ Incorrect checklist and style guide usage
- ▶ Large documents
- ▶ High risk of missing an issue
- ▶ High risk of Refusal To File
- ▶ Demanding timelines

- ▶ **Slow + Complex + Risky**
- ▶ Where have YOU had the biggest issues?



[This Photo](#) by Unknown Author is licensed under [CC BY-SA-NC](#)

Word Templates

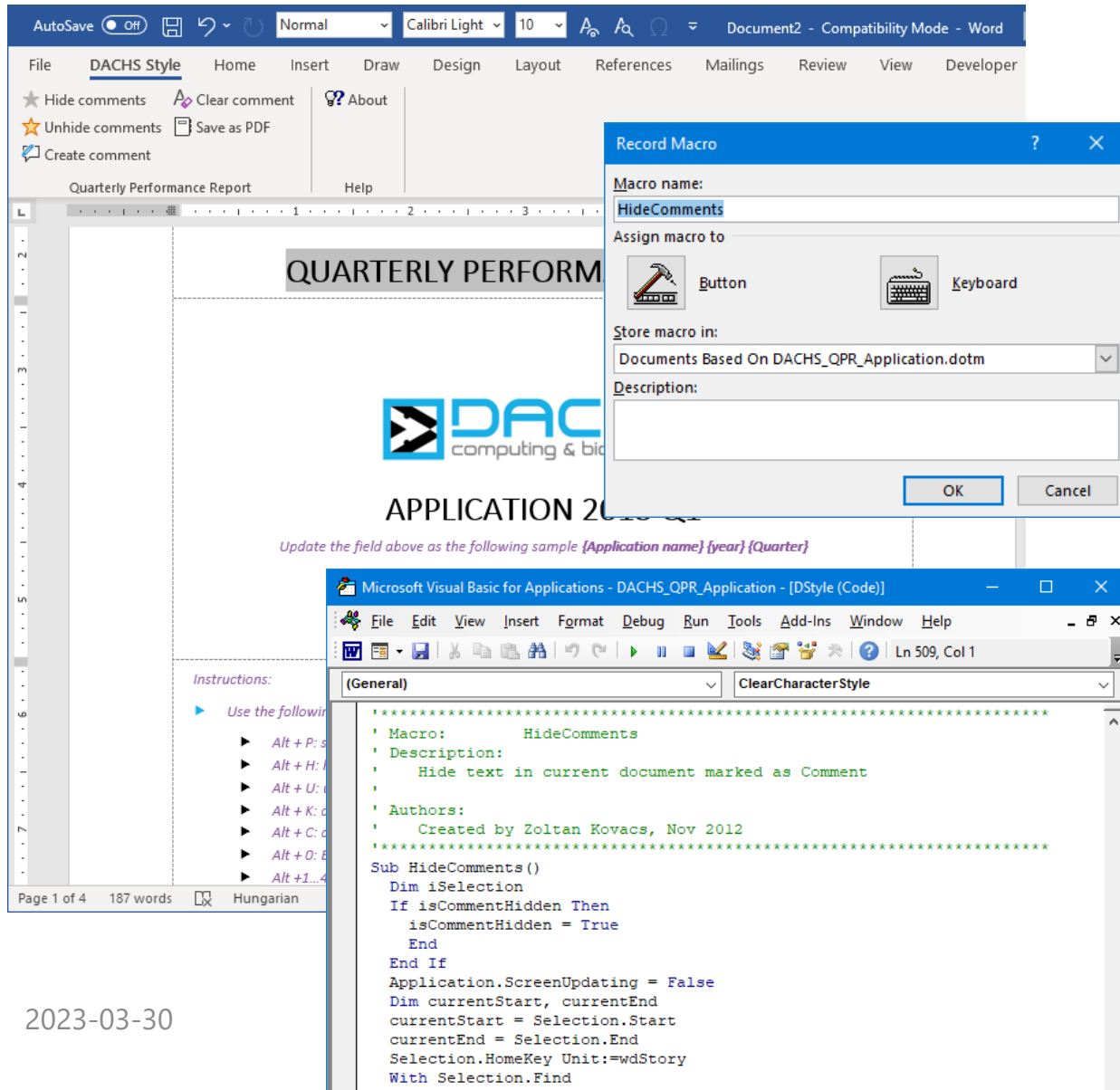
► PROs

- Easy to create from a good sample
- Controlled formatting elements included (paragraph styles, table styles, numberings)

► CONs

- Hard to update existing documents
- Problematic to deploy new updates
- Word senior expertise is still required for the application
- Usage of multiple steps could be time-consuming (table format)

Company Name Drug/Substance Name	Nonclinical Overview
Nonclinical Overview	
1. Cover page	
Document title: Nonclinical Overview	
Company name and address	<Name>, <Address>
Document version and date	<Document version>, <Date>
Regulatory authority(ies) and submission identifier	<Authority> <Sub. identifier>
2. Table of contents	
3. Introduction	
Brief overview of the nonclinical program	
Objective of the Nonclinical Overview	
4. Nonclinical Pharmacology	
Summary of the pharmacology studies conducted	
Description of the pharmacodynamic and pharmacokinetic properties	
Discussion of any relevant findings	



Word Macros

PROs

- ▶ Recorded macros make it easy to repeat complex formatting tasks.
- ▶ No deep development knowledge is necessary to make "smart" tools.
- ▶ Word expertise is not really needed for the application of macros.

CONs

- ▶ VBA code is really slow and unstable during complex task execution (e.g., searching and correction).
- ▶ VBA is an insecure coding solution, sometimes generating a virus scanner false alert.
- ▶ It is still problematic to deploy new updates.

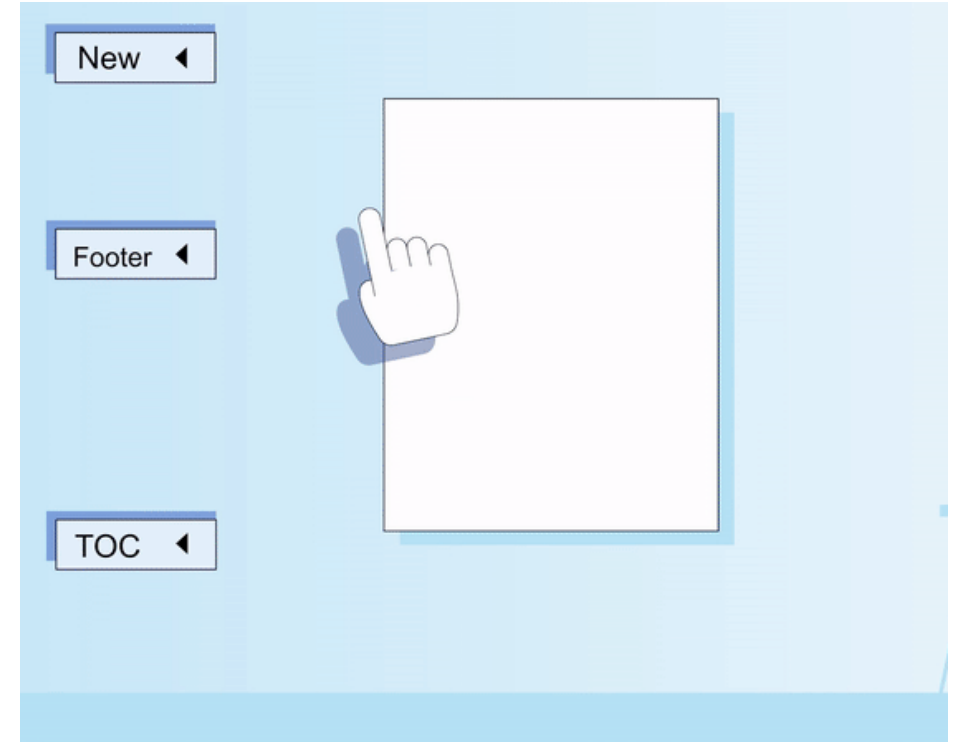
Word Add-Ins

▶ Pros

- ▶ Complex tasks can be achievable
- ▶ Good performance and secure coding solution
- ▶ No Word experience is necessary for application
- ▶ Easy to distribute and update globally
- ▶ Existing documents are manageable

▶ Right examples for application areas

- ▶ Consistency checking - PerfectIt
- ▶ Reference handling – EndNote, Zotero
- ▶ Compliance verification and correction – OnStyle, DocXTools
- ▶ Authoring support – OnStyle



Automatic batch validation and correction for Word files

- Integration with another automated processes/workflow
- Document quality checks on multiple documents
- Automatic corrections
- Detailed report on findings and changes



PDF Files

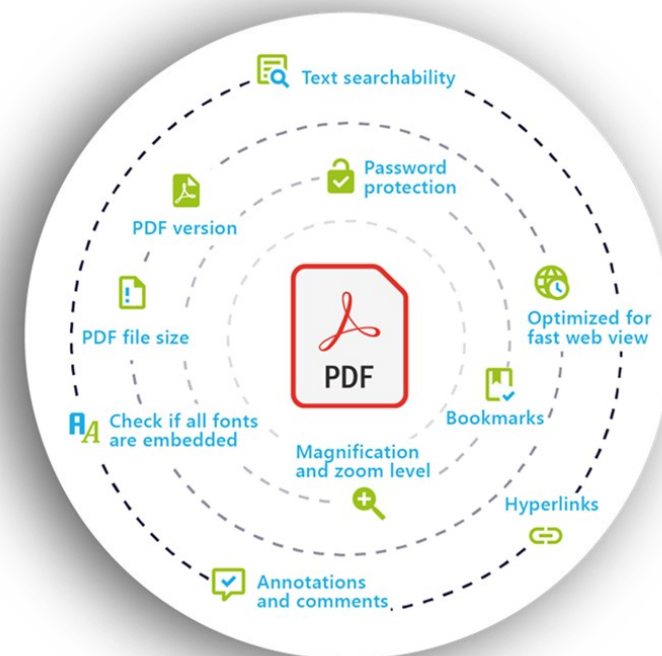
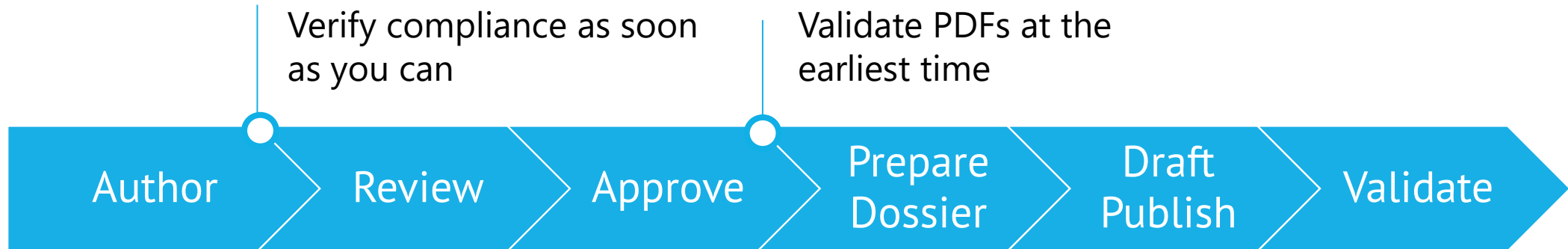
- Adobe Acrobat functions
- Other PDF tools, plug-ins
- Interactive semi-automated batch validation (OnTrack PDF Validation)
- Automatic batch validation

The screenshot displays a software interface for PDF validation. The main window is titled "Clinical Study Report Test File_ref" and shows a document preview of a "DACHS" document. The document content includes "Clinical Development", "AAR111", "Study AAAR111A", and "Test Document". Below this, it lists "Document type: Clinical Study Report", "Document status: Draft", and "Release date:". The footer of the document reads "DACHS Clinical Study Report Confidential Page 2 AAR111A".

On the right side, there is a "Validation Result" panel with tabs for "Manual QC" and "Properties". The "Failed" section is expanded, showing a list of validation errors:

- Bookmarks
 - Bookmark points to the correct page
- Hyperlinks
 - Internal hyperlinks blueed
 - No hyperlink points to a remote destination
 - TOC items point to their correct pages
 - No broken reference hyperlink
 - No blue texts without hyperlinks
 - No blue texts without hyperlinks - ignoring text within square brackets
 - No inactive hyperlink

At the bottom right of the validation panel, there is a "Download Report" button.



- ▶ Use regulatory-specific authoring tools
- ▶ Ensure that you use the right style and formatting standards
- ▶ Automate the identification of issues
- ▶ Automate issue correction
- ▶ Create PDF-ready documents by eliminating known errors



▶ Save Time in QC Review

- ▶ Automate QC checks
- ▶ Get a list of findings in seconds
- ▶ Automate issue correction
- ▶ Use predefined, use-case-specific checklists
- ▶ Create PDF-ready documents by eliminating known errors





Reduce risk

- ▶ Enforce standards
- ▶ Reduce manual steps and time pressure
- ▶ Identify issues and achieve compliance earlier
- ▶ Make sure that technical requirements are met

Speed

- ▶ Automate checks and corrections
- ▶ Reduce rework
- ▶ Work with multiple documents at once
- ▶ Ease communication with comprehensive reports
- ▶ Reuse content in multiple formats for multiple Health Authorities simultaneously

Focus on the content

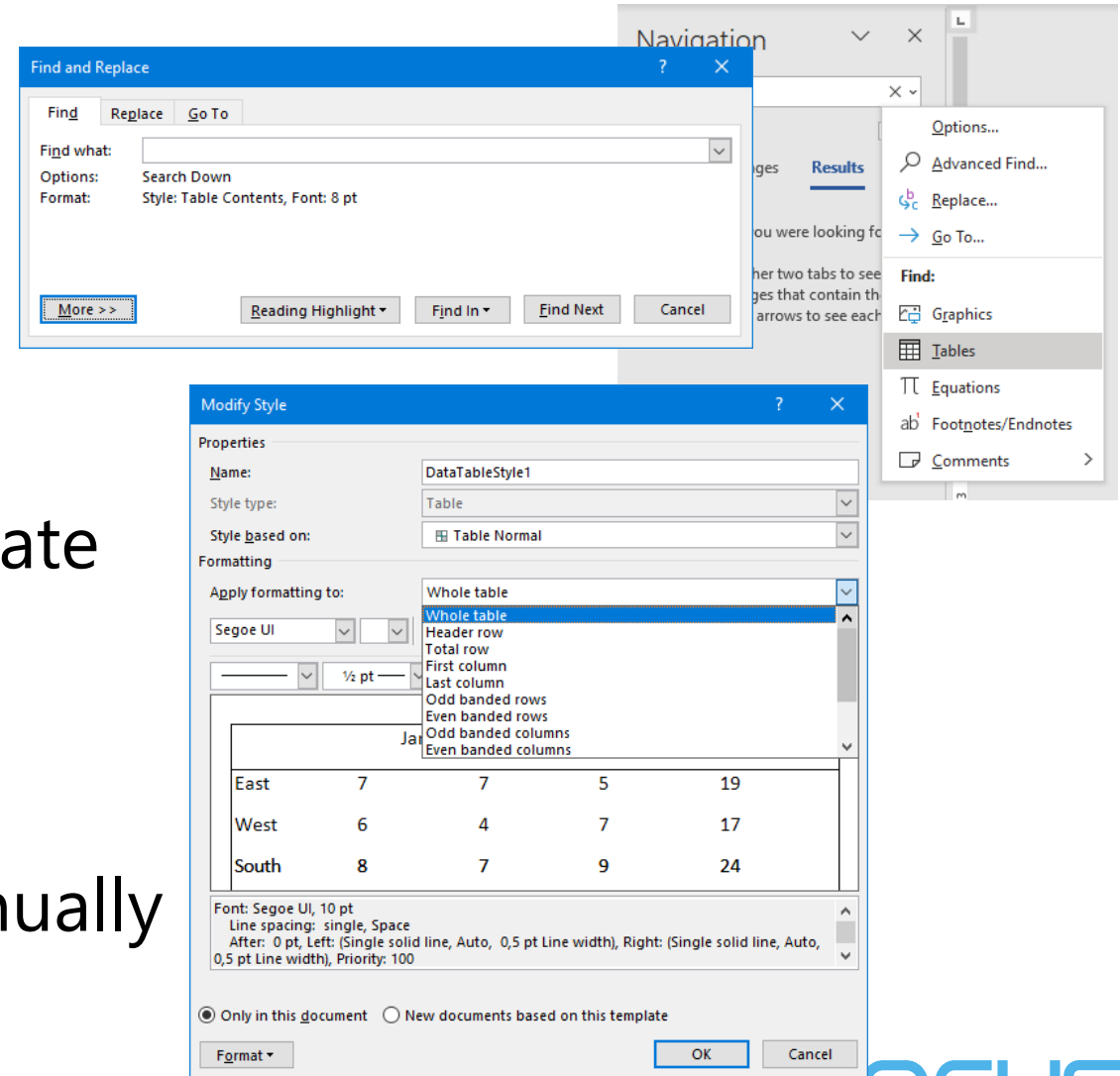
- ▶ Standard tables are very tedious to create properly from external sources, considering
 - ▶ Table borders and header rows
 - ▶ Styles and font formats in cells
 - ▶ Title numbering, captioning, and style
 - ▶ Table sizing and alignment to margin
- ▶ Typical issues
 - ▶ Non-uniform table appearance with improper font format
 - ▶ Incorrect table numbering
 - ▶ Irregular table positioning

▶ How can the typical issues be detected using Word features?

- ▶ Find Tables (one by one)
- ▶ Advanced Find

▶ How can Word Templates help?

- ▶ Prerequisite: have the correct template
 - ▶ Table styles
 - ▶ Paragraph styles
- ▶ Apply simple border formatting
- ▶ Using standard table cell styles manually



▶ How can the typical issues be detected using Word macro features?

- ▶ Macro to find tables (multiple)
- ▶ Advanced search for formatting rules

▶ How can a Word macro help?

- ▶ Add custom bordering and special table format
- ▶ Apply table cell styles with logic
- ▶ Insert smart table captioning

Table 2

Patient	Time	Age	Sex	Weight	Dose	SGOT	SGPT	AP...X
#1	T ₀	70	M	70 kg	400mg	V1*	V5	V9
						V2	V6	V10
						V3	V7	V11
#2						V4	V8	V12
					300mg	V13	V16	V19
						V14	V17	V20
						V15	V18	V21

* V_n = value of a particular test
(Footer text here; all footnotes should end with a period.)

Patient	Time	Age	Sex	Weight	Dose	SGOT	SGPT	AP...X
#1	T ₀	70	M	70 kg	400mg	V1*	V5	V9
	T ₁					V2	V6	V10
	T ₂					V3	V7	V11
#2	T ₃					V4	V8	V12
	T ₁₀					V13	V16	V19
	T ₂₁					V14	V17	V20
	T ₃₂					V15	V18	V21

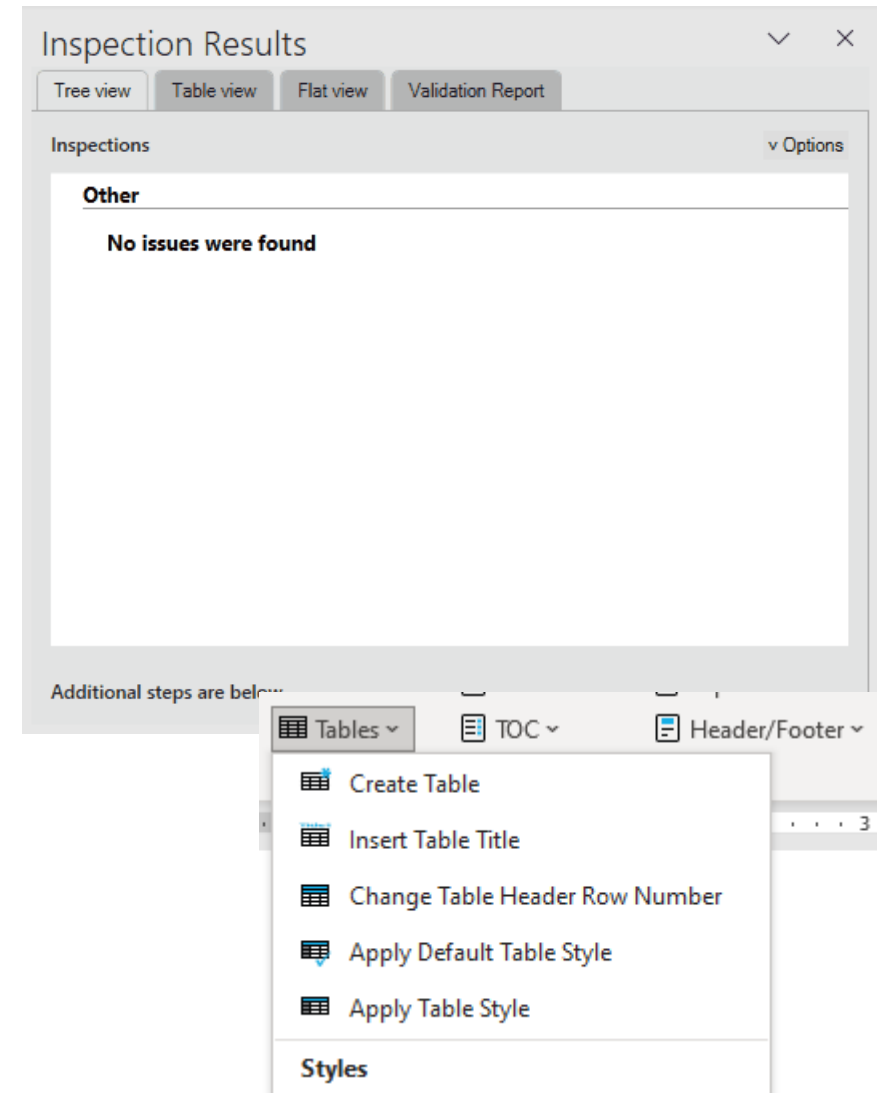
* V_n = value of a particular test

▶ How can these issues be detected using OnStyle features?

- ▶ Table Not Fitting to Page
- ▶ Table Header Row Not Repeating
- ▶ Table with Row Break across Pages
- ▶ Table with Small Font Size
- ▶ Incorrect Caption, Missing Caption, Orphan Caption
- ▶ Receding Caption, Empty Caption

▶ How can OnStyle help?

- ▶ Create a standard table
- ▶ Insert a standard table title
- ▶ Transform existing table by
 - ▶ Applying the selected Table Style
 - ▶ Using the default table style for multiple tables
- ▶ Change the number of header rows and reformat them



- ▶ Hyperlink issues are very hard to detect
- ▶ Typical issues
 - ▶ Wrong or missing hyperlink target
 - ▶ Text looks like a hyperlink, but the link is missing
 - ▶ Hyperlink looks like normal text
- ▶ How can these issues be detected manually?
- ▶ How can these issues be detected using Word features?
- ▶ How can OnStyle help?
 - ▶ Inspection and correction modules
 - ▶ Export all hyperlinks

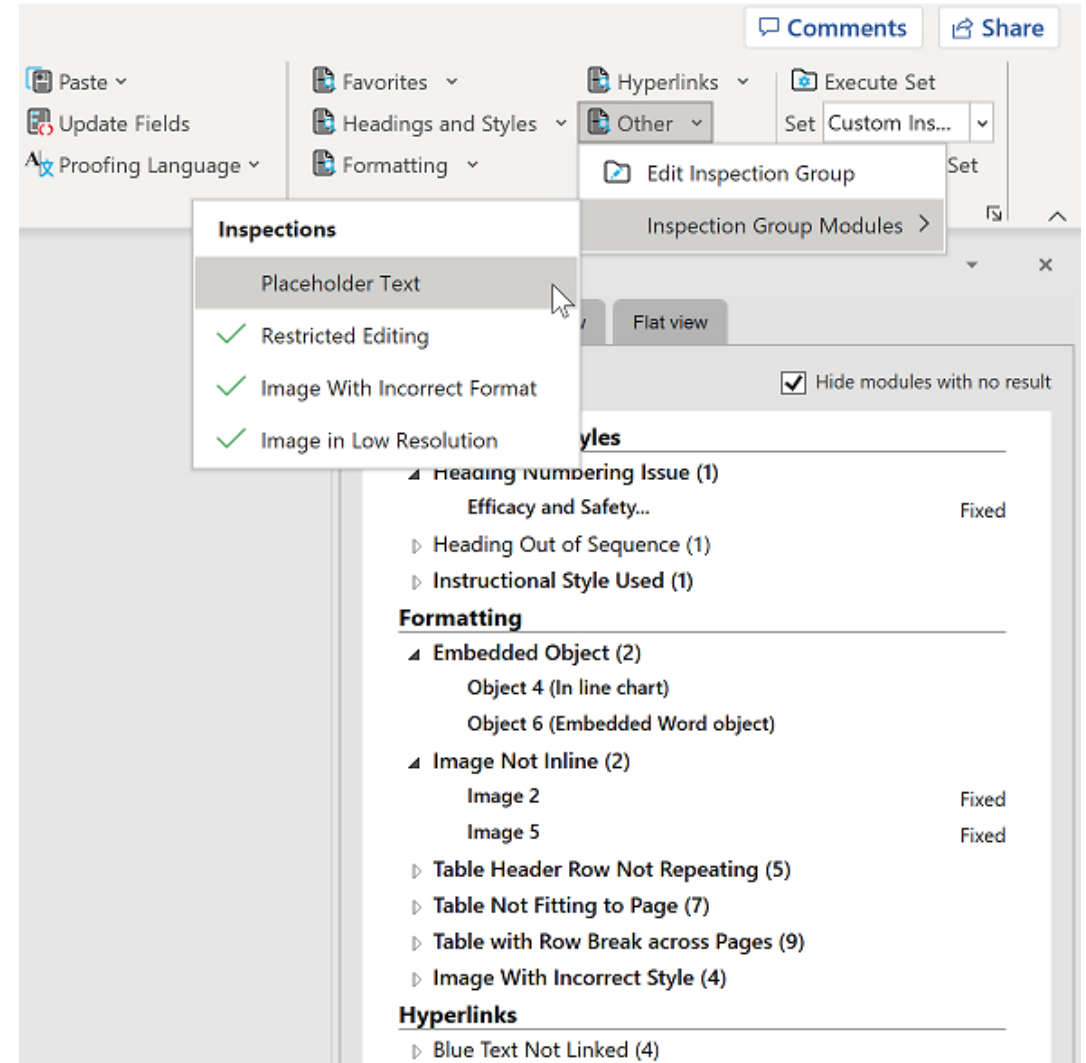
- ▶ Abbreviation table is mandatory in large documents
- ▶ How to create it?
 - ▶ Manually, searching all used abbreviations in the document
 - ▶ Copy and paste an existing table from another document
 - ▶ Try to collect the abbreviations and their descriptions with regular expression search
 - ▶ Use an add-in, like OnStyle
- ▶ Challenges
 - ▶ To meet all rules and requirements
 - ▶ To collect automatically the abbreviation descriptions



- ▶ Proven Word plug-in
- ▶ Customized for Life Sciences
- ▶ Controlled, supported authoring
- ▶ Automated QC checks
- ▶ Automated fixes
- ▶ Improved document quality
- ▶ Comprehensive validation report

- ▶ Configurable Ribbon with powerful authoring tools
- ▶ Predefined authoring settings ensure that you use the right style and formatting standards
- ▶ Automated validation identifies and lists the deviations from standards
- ▶ The tool navigates you to the issues and gives guidance for correction
- ▶ Controlled, automated issue correction
- ▶ Document updates to the newest standard or multiple formats with a single click

- Submission-specific inspections
- Configurable inspection sets
- Issues are listed and navigated to
- Number of found issues is indicated
- Automated correction for issue types in bold
- Issues can be corrected one by one or all at once
- Status of the issues is indicated



- 1) [Abbreviation](#)
- 2) [Blue Text Not Linked](#)
- 3) [Character Formatting Applied](#)
- 4) [Character Style Applied](#)
- 5) [Comment Available](#)
- 6) [Corrupt Style Alias](#)
- 7) [Cross-Reference Issue](#)
- 8) [Document Revisions](#)
- 9) [Embedded Object](#)
- 10) [Empty Key Property](#)
- 11) [Empty Page](#)
- 12) [Empty Paragraph](#)
- 13) [External Link Formatting](#)
- 14) [Harvard Style Reference](#)
- 15) [Heading Numbering Issue](#)
- 16) [Heading or Title with Break](#)
- 17) [Heading Out of Sequence](#)
- 18) [Heading Whitespace](#)
- 19) [Hidden Text Available](#)
- 20) [Highlighted Text](#)
- 21) [Hyperlink to External Document](#)
- 22) [Hyperlink with No Hyperlink Style](#)
- 23) [Image in Low Resolution](#)
- 24) [Image Not Inline](#)
- 25) [Image with Incorrect Format](#)
- 26) [Image with Incorrect Style](#)
- 27) [Incorrect Caption](#)
- 28) [Incorrect List Format](#)
- 29) [Instructional Style Used](#)
- 30) [Internal Hyperlink Not Set](#)
- 31) [Internal Hyperlink Target Mismatch](#)
- 32) [Internal Hyperlink with No Target](#)
- 33) [Internal Reference Document](#)
- 34) [Invalid Symbol](#)
- 35) [Language Issue](#)
- 36) [Manual Page Break](#)
- 37) [Narrative Text Formatting Issue](#)
- 38) [Non-black Text](#)
- 39) [Nonstandard Page Layout](#)
- 40) [Nonstandard Style Used](#)
- 41) [Obsolete Cross-Reference](#)
- 42) [Paragraph Formatting Applied](#)
- 43) [Placeholder Text](#)
- 44) [Protected Document](#)
- 45) [Read-Only Mode](#)
- 46) [Repeating Whitespaces](#)
- 47) [Restricted Access](#)
- 48) [Restricted Editing](#)
- 49) [Special Character](#)
- 50) [Special Keyword Used](#)
- 51) [Standard Style Modified](#)
- 52) [Strikethrough Text](#)
- 53) [Symbol in TOC](#)
- 54) [Table Header Row Not Repeating](#)
- 55) [Table Not Fitting to Page](#)
- 56) [Table with Row Break across Pages](#)
- 57) [Table with Small Font Size](#)
- 58) [Track Changes](#)
- 59) [Unused Bookmark](#)
- 60) [Unused Nonstandard Style](#)
- 61) [Watermark Available](#)
- 62) [Web Link Available](#)



- ▶ Health authority–specific PDF validation
- ▶ Many documents validated at the same time
- ▶ Predefined, use-case-specific checklists
- ▶ List of findings in seconds
- ▶ Easy navigation to issues
- ▶ Manual QC support
- ▶ Comprehensive validation report

▶ How Does OnTrack PDF Validation Work

The screenshot displays the OnTrack PDF Validation interface, divided into several main sections:

- Navigation:** A sidebar on the left shows a hierarchical folder structure under 'Team 1 (4)'. Callout: "Workspaces and category folders".
- Status:** A table at the bottom left lists documents with their validation status. Callout: "Document's validation status".

Status	Document Name	Owner
4d ✓	Clinical Study Report Compliant.pdf	Quality Analyst-1
10d ✗	Clinical Study Report_PDF_Validation (1).pdf	Quality Manager-1
4d ✗	Clinical Study Report...	
- Preview:** The central area shows a PDF document with a navigation pane on the left. Callout: "Navigation to Issues".
- Folder Configuration:** A top-right panel for document settings.
- Validation Result:** A right-hand panel showing a list of issues. Callout: "Immediate validation result".
 - Failed (toggle)
 - Pages
 - ✗ First page and headers do not indicate 'draft'
 - Bookmarks
 - ✗ Bookmark points to the correct page
 - ✗ Bookmark's title not found as searchable text on target page - it could be present fully or partially as image only
 - Hyperlinks
 - ✗ Internal hyperlinks blueed
 - ✗ Hyperlink appearance is not valid
 - ✗ No hyperlink points to a remote destination
 - ✗ TOC items point to their...
 - ✗ No broken reference hyp...
- Manual QC:** A section for manual quality control. Callout: "Downloadable PDF report".
- Properties:** A section for document properties.

Additional callouts include "Bulk file upload and instant validation" pointing to the "Upload" button at the bottom left, and "Quality Manager-1 - 03/03/2023 10:56:38 This is not an issue." pointing to a comment box in the Validation Result panel.

Configurable Validation Rules in OnTrack

Navigation

- Team 1 (5)
 - M-5-Clinical Study Reports (4)
 - M-4-Nonclinical Study Reports
 - M-3-Quality
 - M-2-Overview and Summary (1)
 - Quality Overall Summary
 - Nonclinical Overview
 - Nonclinical Summary
 - Clinical Overview
 - Clinical Summary
 - Information

Folder Configuration

Select All Search

Status	Verification Code	Label	Description
<input checked="" type="checkbox"/>	MAN.MARKETING-TEAM1.1	Header ranges are consistent	Header ranges should be consistent in the document.
<input checked="" type="checkbox"/>	MAN.MARKETING-TEAM1.2	Artifact names are correct	Correct Artifact should be selected and should match with document content.
<input checked="" type="checkbox"/>	MAN.MARKETING-TEAM1.3	Attributes are completed	The attributes of each document should be correctly completed, to help with accurate auto-naming (e.g. Investigator Name, document date, etc.).
<input type="checkbox"/>	PDF.ANNO.1	No comments	Document contains one or more comments.
<input checked="" type="checkbox"/>	PDF.ANNO.2	No annotations	Document contains one or more annotations.
<input type="checkbox"/>	PDF.ANNO.3	No digital signatures	Document contain one or more digital signatures.
<input checked="" type="checkbox"/>	PDF.ANNO.4	No watermark	Watermark applied on pages.
<input checked="" type="checkbox"/>	PDF.BMRK.1	Bookmarks are expanded until the defined level	Bookmarks are not expanded until the first level or they are over expanded.
<input type="checkbox"/>	PDF.BMRK.10	No symbols in bookmark	Document does not contain symbols in bookmarks

Validation Result Manual QC Properties

Identified header ranges: 2-40

Header ranges are consistent +

Artifact names are correct +

^ +

- Yes
- No
- N/A

Manual QC support

Workspace admin can configure validation rule sets

Multiple folders with specific validation rules

20 Upload Delete All Modified by Quality Manager-1 28/03/2023 18:22:37 Save Save

- 1) Text is searchable
- 2) PDF file size does not exceed configured limit
- 3) PDF contents can be processed successfully
- 4) PDF is not protected by open password
- 5) No certificate protection
- 6) PDF version is correct
- 7) "Fast Web View" option is activated
- 8) No security (document access) restriction is set
- 9) All used fonts have been embedded
- 10) No Track Changes
- 11) Navigation Tab Setting
- 12) Page Layout is set to Default
- 13) Magnification is set to Default
- 14) Document open to page 1 or TOC
- 15) PDF contains only pages with the configured sizes
- 16) First page orientation is portrait
- 17) No blank page
- 18) Sequential page numbering
- 19) First page and headers do not indicate 'draft'
- 20) No text on side margins
- 21) Correct scan resolution
- 22) Bookmarks are expanded until the defined
- 23) Number of bookmark levels does not exceed maximum limit
- 24) Bookmark nesting is correct
- 25) Bookmark has title and destination
- 26) Magnification of the bookmarks is set to inherit zoom
- 27) No multiple action bookmark
- 28) There are bookmarks
- 29) Provide bookmarks for each item listed in TOC
- 30) First bookmark leads to first page
- 31) No symbols in bookmark
- 32) Bookmark points to an existing page
- 33) Bookmark points to the correct page
- 34) Internal hyperlinks blued
- 35) No broken reference hyperlink
- 36) Relative paths are used in hyperlinks
- 37) No external hyperlinks to websites
- 38) Magnification of the hyperlinks is set to inherit zoom
- 39) No multiple action hyperlink
- 40) No blue texts without hyperlinks
- 41) No blue texts without hyperlinks - ignoring text within square brackets
- 42) Hypertext linked TOC is included
- 43) No inactive hyperlink
- 44) Hyperlink points to an existing page
- 45) Hyperlink points to the correct page
- 46) No hyperlink points to a remote destination
- 47) TOC items point to their correct pages
- 48) Sequential TOC section numbering
- 49) Provide TOC item for each bookmark
- 50) No comments
- 51) No annotations
- 52) No digital signatures
- 53) No watermark

▶ You learned that:

- ▶ You can save a lot of time and reduce the risk of non-compliance.
- ▶ Early validation is feasible in the submission process on both Word and PDF files.
- ▶ There are powerful automation tools with lot of checks and fixes.
 - ▶ See OnStyle & OnTrack





Thank you for your attention

More info: <https://dachs.ch>

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zoltan.kovacs@dachs.ch