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Efficiency in Action: Automating Bookmarking for CRFs and Other Regulatory Submission Documents

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ABSTRACT

Bookmarking Case Report Forms (CRFs) for regulatory submissions is a critical yet often labor-intensive task for statistical programmers. Manual bookmarking in Adobe Acrobat Pro™ is time-consuming, repetitive, and prone to human error, especially for large, multi-level documents. This paper presents a clear, step-by-step workflow for automating CRF bookmarking using the TRS toolbox™ (formerly ISI toolbox) plug-in for Adobe Acrobat Pro. By leveraging the toolbox's import/export functionality and Excel templates, programmers can efficiently generate, edit, and apply complex bookmark structures with minimal manual intervention. This approach accelerates the submission preparation while improving accuracy, reproducibility, and compliance with regulatory requirements. The workflow is illustrated with practical procedures, template examples, and guidance for integrating screenshots, making it accessible for programmers seeking to streamline their CRF bookmarking.

INTRODUCTION

Statistical programmers play a pivotal role in preparing regulatory submission documents, including the creation of navigable, well-structured bookmarks in CRFs. Regulatory agencies such as the FDA and EMA require electronic submissions to be easily navigate, with bookmarks that reflect the document's logical structure. Traditionally, programmers have relied on manual bookmarking in Adobe Acrobat Pro—a process that is not only tedious but also susceptible to inconsistencies and errors, particularly when dealing with large or complex CRFs.

The TRS toolbox, a robust plug-in for Adobe Acrobat Pro, offers a suite of tools designed to automate and standardize PDF management tasks. Of particular interest is its ability to export and import bookmark structures via Excel templates, enabling batch creation and editing of bookmarks. This paper details a practical workflow for automating CRF bookmarking, tailored to the needs of statistical programmers, and demonstrates how this approach can transform a labor-intensive process into a streamlined, reproducible task.

OVERVIEW OF THE TRS TOOLBOX

The TRS toolbox (formerly ISI toolbox) is a comprehensive plug-in for Adobe Acrobat Pro, developed to automate repetitive PDF tasks commonly encountered during regulatory submission preparation. As a prerequisite, users must have Adobe Acrobat Pro installed, as the TRS toolbox operates as an integrated plug-in within the Acrobat environment. The availability and installation of the TRS toolbox may vary by organization and is typically managed through an internal software distribution portal or coordinated through the company's information technology (IT) team.

Key features relevant to CRF bookmarking include:

- Export/Import Tool: Export bookmarks and hyperlinks to Excel or CSV, edit them, and re-import to apply changes.
- Batch Processing: Apply bookmark templates across multiple documents.
- Bookmark Editor and Auditor: Edit, QC, and validate bookmarks efficiently.

Among these features, the Export/Import functionality is particularly valuable because it enables bookmark creation to be driven by a structured, reviewable Excel template rather than manual interaction within the PDF.

WORKFLOW OVERVIEW

This section outlines the end-to-end workflow used to automate CRF bookmarking using the TRS toolbox and Excel templates. The approach focuses on exporting a correctly structured bookmark template, populating only the key fields required to define Visit-level and Domain-level bookmarks, and importing the completed template back into the CRF PDF. A final quality control step ensures that the generated bookmarks are accurate, navigable, and submission-ready.

Although this paper uses the eCRF as the primary example, the same Excel-driven bookmarking and validation approach can be applied to other regulatory submission documents. This includes, but is not limited to, clinical study reports (CSRs), protocols, statistical analysis plans (SAPs), and appendices, where structured bookmark hierarchies and navigation validation are similarly required.

EXPORTING AN EMPTY BOOKMARK TEMPLATE

The purpose of this step is to guide the user on how to obtain the Excel template required for CRF bookmarking using the TRS toolbox. This template will later be used to define the final bookmark structure that is applied to the CRF for regulatory submission.

In theory, a blank Excel file with the required columns could be created manually. However, this approach is error prone and inefficient, as the column names, formats, and expected structure must exactly match what the TRS toolbox requires during import. A more reliable and efficient approach is to export a bookmark template directly from the PDF using the Export & Import function. This ensures the Excel file is correctly structured and immediately ready for use.

In many cases, the raw annotated CRF exported from the EDC system already contains basic bookmarks, such as form names or page numbers. These existing bookmarks can be reused as a starting point. Exporting them into Excel allows the user to build upon the existing structure and complete the CRF bookmarking required for submission, rather than starting from scratch.

STEP BY STEP INSTRUCTIONS

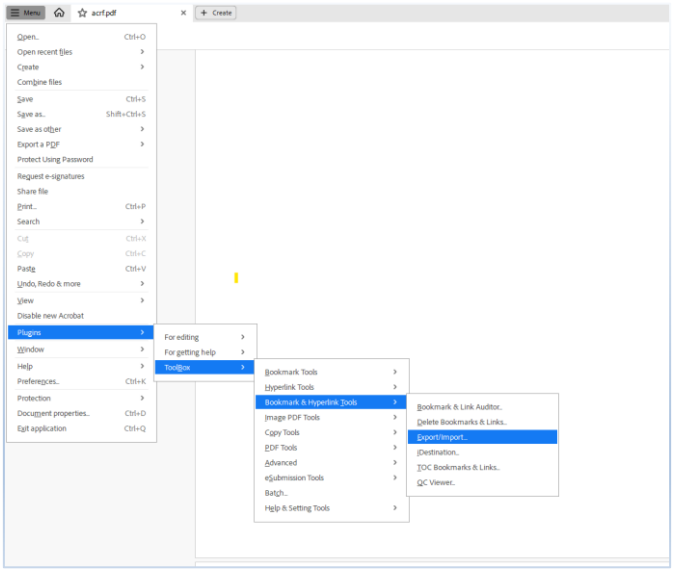
1. Open the CRF PDF in Adobe Acrobat Pro.

   Note: If the CRF does not contain any bookmarks, at least one temporary bookmark must be created before exporting. The export process requires an existing bookmark to generate the Excel template. A simple test bookmark (for example, pointing to the first page of the document) is sufficient and can be removed later.

2. Open the TRS Toolbox and navigate to:

   Menu→Plugins→Toolbox → Bookmark & Hyperlink Tools→ Export & Import. (See Display 1. TRS Toolbox Export & Import Menu Path in Adobe Acrobat Pro).

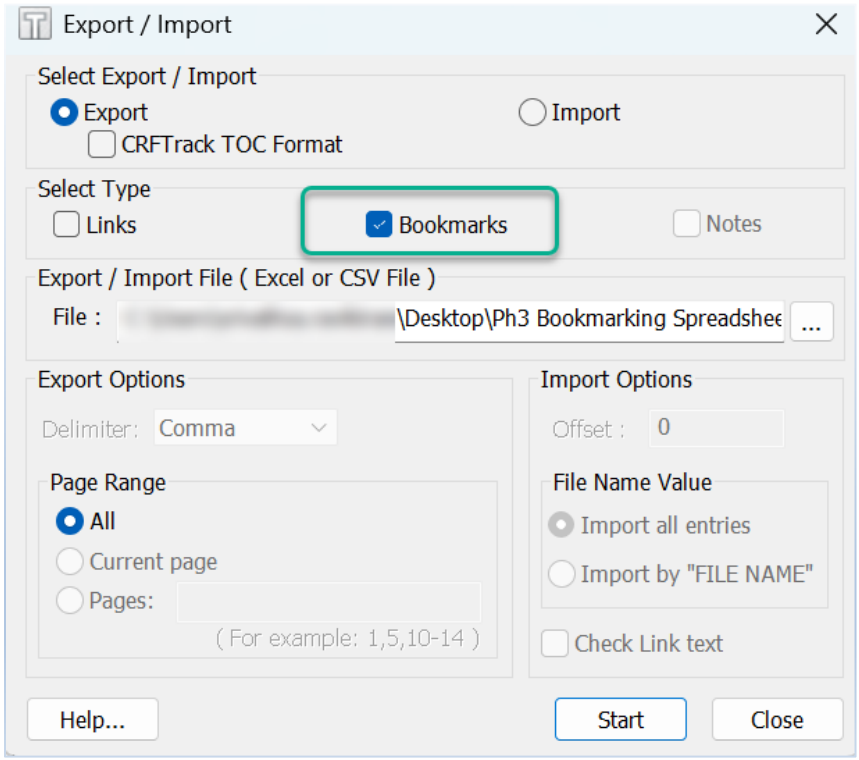
Display 1. TRS Toolbox Export & Import Menu Path in Adobe Acrobat Pro



3. In the Export & Import dialog box, select Export.
4. Check Bookmarks only.

   Do not select Links for this step. (see Display 2. TRS Toolbox Export/Import Dialog with Bookmarks Selected (Export Mode))

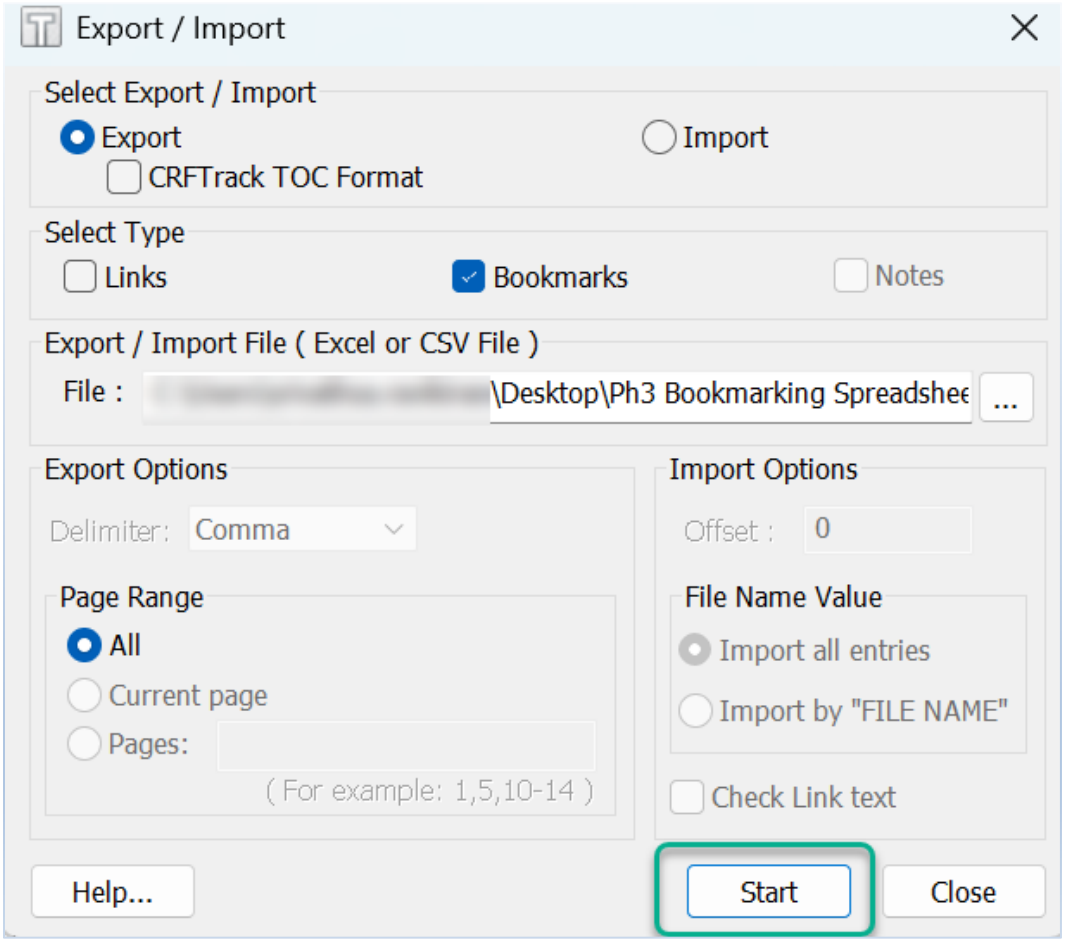
Display 2. TRS Toolbox Export/Import Dialog with Bookmarks Selected (Export Mode)



5. Select Excel (.xls) as the output format.
6. Click Browse and choose a location to save the file.

   Use a clear file name, for example: CRF_Bookmark_Template.xls.
7. Set Page Options to All.
8. Click Start to export the bookmarks. (See Display 3. Export Bookmarks to Excel Using the Start Button)

Display 3. Export Bookmarks to Excel Using the Start Button



9. Open the exported Excel file and verify that it contains the bookmark related columns (for example, bookmark title, hierarchy level, destination page or named destination, and display attributes).

At this point, the Excel file serves as the bookmark template. The file may be mostly empty, or it may already contain form level or page level bookmarks exported from the raw annotated CRF. In the next step, this template will be completed and refined to meet the CRF bookmarking requirements for regulatory submission.

POPULATING THE EXCEL TEMPLATE

The exported Excel template contains multiple columns required by the TRS toolbox. For CRF bookmarking, most columns either use a constant value across all rows or are intentionally left blank. Only a small subset of columns must be populated by the user to define the Visit-level and Domain-level bookmark structure.

Table 1. Instructions for Populating the Excel Bookmark Template provides clear guidance on how each column should be populated when creating CRF bookmarks. The table below focuses on practical usage rather than documenting every available column, highlighting only what must be populated, what should be carried across rows, and what can remain blank.

Table 1. Instructions for Populating the Excel Bookmark Template

Column Name	Description	How to Populate for CRF Bookmarking
FILE_NAME	File name and path of the CRF PDF.	Enter the CRF PDF path (for example, C:\Users\...\ph3.pdf) and carry this value to all rows.
TYPE	Indicates whether the row is a bookmark or link.	Enter “BOOKMARK” and carry this value to all rows.
INDENT_SRCPAGE	Bookmark hierarchy level.	Populate. Use this column to define hierarchy: • Visit-level bookmarks: parent levels (for example, 1, 1.02, 1.03). • Domain-level bookmarks: nested under the visit (for example, 1.02.01, 1.02.02).
TITLE/TEXT	Visible bookmark name.	Populate. Enter bookmark names based on CRF structure: • Visit-level: Visit name (for example, PH3W4, PH3W12). • Domain-level: Form or domain name (for example, Laboratory Tests, Demographics).
ACTION	Bookmark action type.	Enter “Goto_View_Internal” and carry this value to all rows.
MAGNIFICATION	Zoom behavior for destination page.	Enter “INHERIT_ZOOM” and carry this value to all rows.
DEST_PAGE	Destination page number in the PDF.	Populate. Enter the page number the bookmark should navigate to. Page numbers from the annotated CRF can be reused and updated as needed.
DEST_FILE	Destination file reference.	Leave blank for CRF bookmarks within the same PDF.
FULL_PATH	Absolute destination file path.	Leave blank.
ZOOM	Fixed zoom percentage.	Enter ‘0’ and carry this value to all rows.
DEST_RECT_L	Destination rectangle left coordinate.	Enter ‘0’ and carry this value to all rows.
DEST_RECT_R	Destination rectangle right coordinate.	Enter ‘0’ and carry this value to all rows.

Column Name	Description	How to Populate for CRF Bookmarking
DEST_RECT_B	Destination rectangle bottom coordinate.	Enter ‘0’ and carry this value to all rows.
DEST_RECT_T	Destination rectangle top coordinate.	Enter ‘792’ and carry this value to all rows.
LEFT	Source rectangle left coordinate.	Enter ‘NA’ and carry this value to all rows.
RIGHT	Source rectangle right coordinate.	Enter ‘NA’ and carry this value to all rows.
TOP	Source rectangle top coordinate.	Enter ‘NA’ and carry this value to all rows.
BOTTOM	Source rectangle bottom coordinate.	Enter ‘NA’ and carry this value to all rows.
COLOR	Bookmark display color.	Enter ‘RGB(0,0,0)’ and carry this value to all rows.
STYLE_WIDTH	Bookmark text style.	Enter ‘Plain’ and carry this value to all rows.
OPEN_IN_WINDOW	Destination window behavior.	Enter ‘Window set by user preference’ and carry this value to all rows.
OPEN_CLOSE	Bookmark expanded or collapsed state.	Enter OPEN for Visit-level bookmarks and N/A for Domain-level bookmarks.
NAMED_DEST	Named destination reference.	Leave blank
ABSOLUTE_PATH	Absolute vs relative path indicator.	Enter ‘0’
HIGHLIGHT_STYLE	Link highlight behavior.	Leave blank.
LINE_STYLE	Link line style.	Leave blank.

COLUMNS THAT DRIVE CRF BOOKMARK CREATION

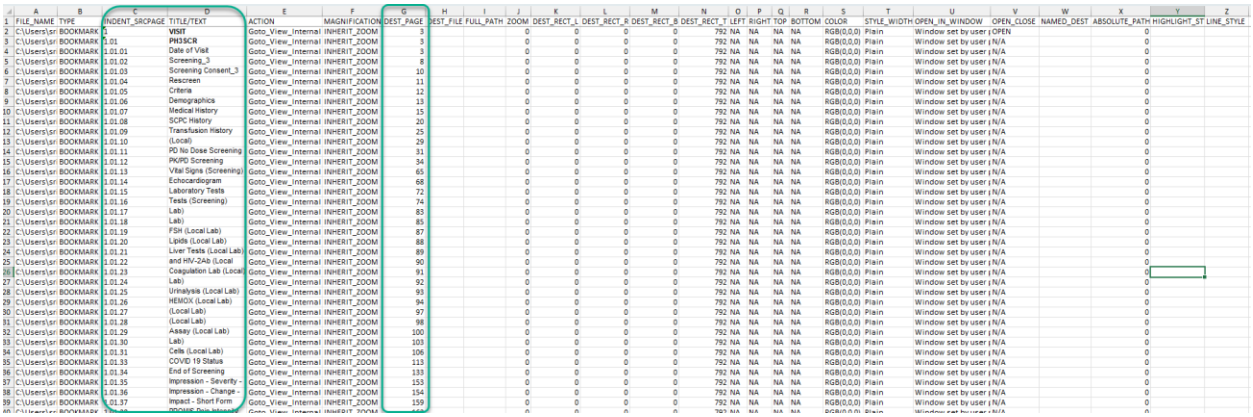
When creating CRF bookmarks by Visit and Domain, the user primarily works with the following columns:

- INDENT_SRCPAGE – defines Visit and Domain level hierarchy
- TITLE/TEXT – defines the bookmark names displayed in the PDF
- DEST_PAGE – defines where each bookmark navigates in the CRF

All other columns either use constant values carried across the template or are intentionally left blank.

An example of a populated Excel bookmark template is shown below (Display 4. Example of a Populated Excel Bookmark Template Highlighting Key User-Input Columns). In this example, the key columns requiring user input are highlighted within the green rectangle to clearly illustrate which fields must be populated to define the CRF bookmark structure.

Display 4. Example of a Populated Excel Bookmark Template Highlighting Key User-Input Columns



In addition to manual editing, the Excel bookmark template can also be prepared programmatically. Because the template follows a structured, tabular format, it can be generated or populated using standard scripting or programming approaches (for example, from metadata, specifications, or controlled lists). This allows bookmark structures to be created, updated, or reused in a consistent and reproducible manner, particularly for large documents or repeated submissions. Once generated, the populated template can be imported into the PDF using the same TRS toolbox workflow described above.

IMPORTING THE POPULATED TEMPLATE

Once the Excel template has been populated with the required Visit level and Domain level bookmarks, the next step is to import the template back into the CRF PDF to generate the bookmarks automatically.

Before importing, it is recommended to remove any existing bookmarks in the PDF to avoid duplication or conflicts. This ensures that the final bookmark structure is driven entirely by the Excel template.

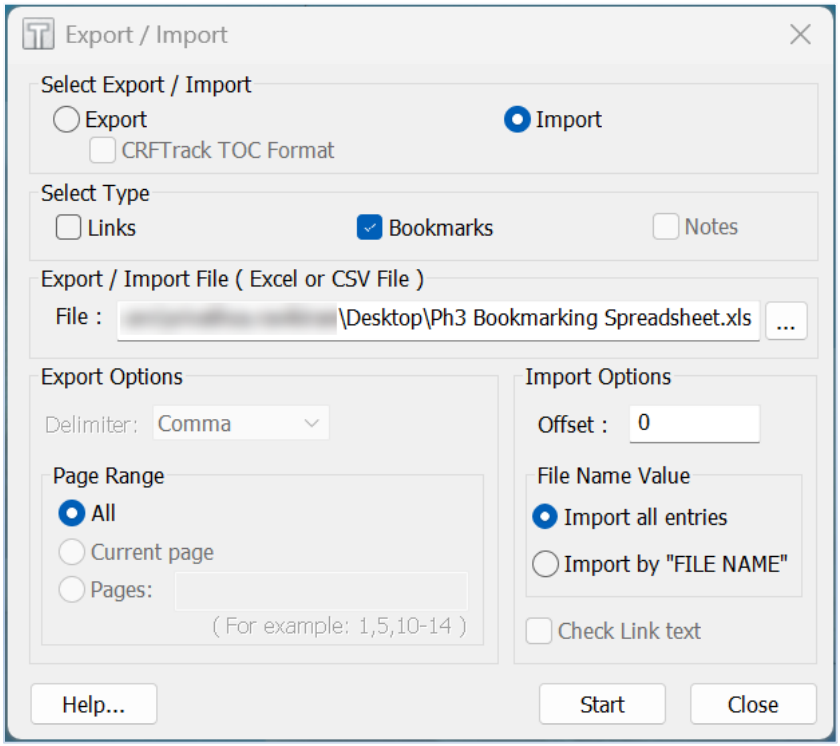
STEP BY STEP INSTRUCTIONS

1. Open the CRF PDF in Adobe Acrobat Pro.
2. If bookmarks already exist in the document, use the TRS toolbox to delete them:
    - Navigate to Menu → Plugins → Toolbox → Bookmark & Hyperlink Tools → Delete Bookmarks
    - Confirm deletion
3. Open the TRS Toolbox and navigate to:

    Menu → Plugins → Toolbox → Bookmark & Hyperlink Tools → Export & Import. (see Display 1. TRS Toolbox Export & Import Menu Path in Adobe Acrobat Pro)
4. Select Import.

    Choose Excel (.xls) as the input format and browse to the populated Excel bookmark template.
5. Confirm that Bookmarks is selected for import.
6. Click Start to import the bookmarks. (see Display 5. Import Bookmarks from Excel Using the Export/Import Dialog (Import Mode))

Display 5. Import Bookmarks from Excel Using the Export/Import Dialog (Import Mode)



7. Once the import is complete, review the bookmark pane in the PDF to confirm that the Visit level and Domain level bookmarks have been created as expected.

At the end of this step, the CRF PDF contains a fully populated bookmark structure generated directly from the Excel template.

QUALITY CONTROL AND FINALIZATION

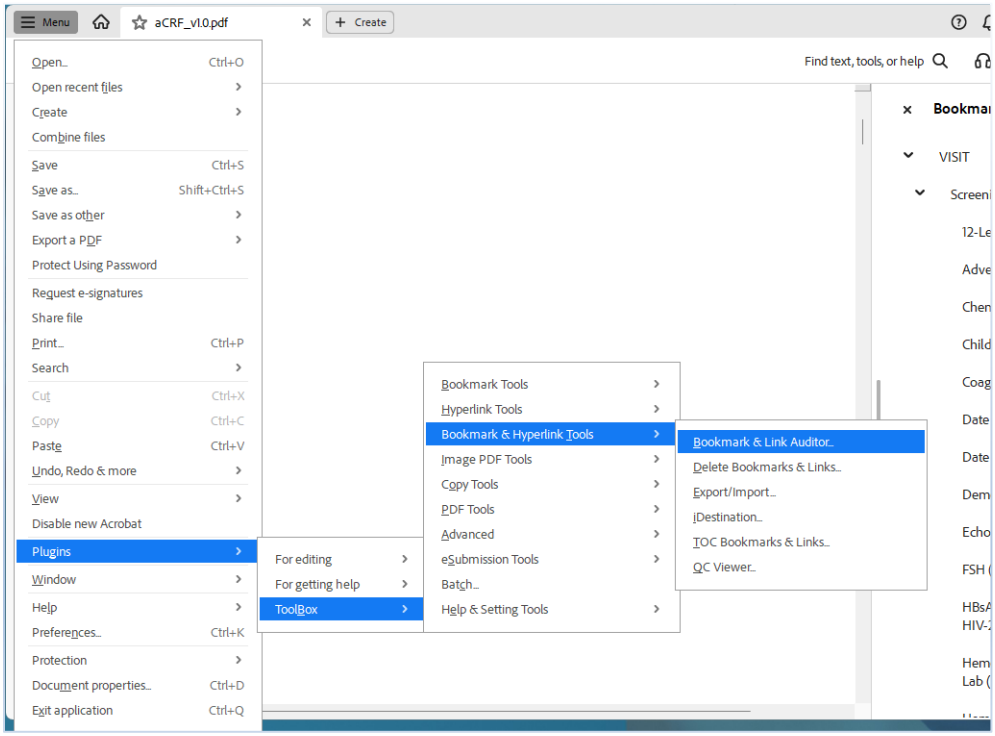
After importing the bookmarks, a quality control (QC) step is performed to ensure that all bookmarks function correctly and meet submission requirements. QC focuses on both structural accuracy and navigation behavior.

The TRS toolbox provides built in tools that allow bookmarks to be reviewed efficiently without manually clicking through each one.

STEP BY STEP INSTRUCTIONS

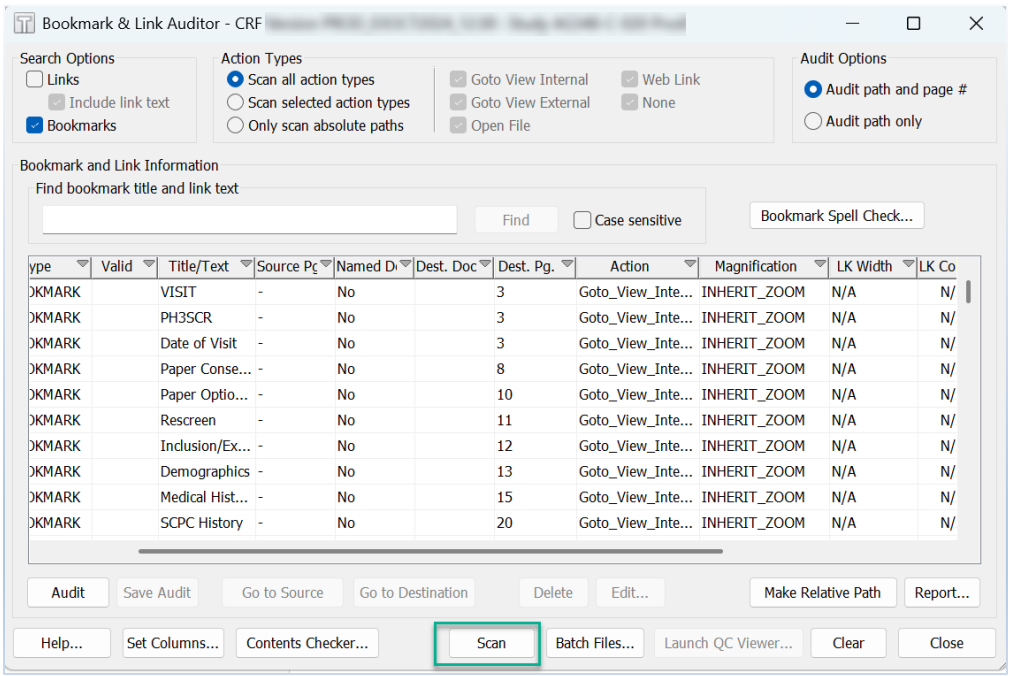
1. Open the Menu → Plugins → Toolbox →Bookmark & Link Auditor from the TRS Toolbox. (see Display 6. Launching Bookmark & Link Auditor from TRS Toolbox)

Display 6. Launching Bookmark & Link Auditor from TRS Toolbox



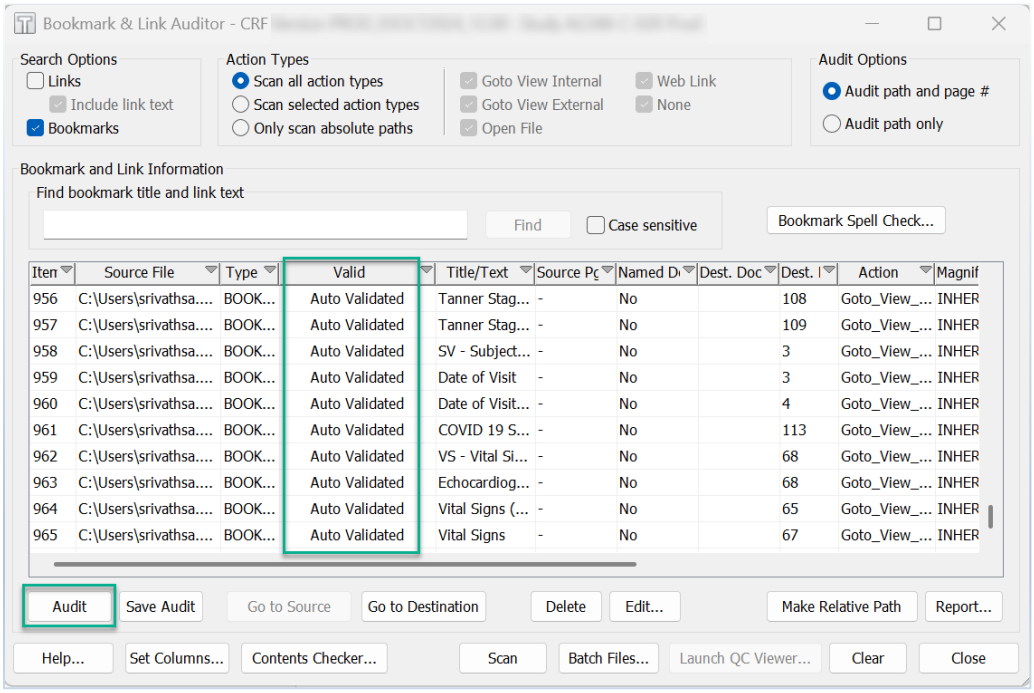
2. Click on the “Scan” to load all “Bookmarks” into the Auditor Window. (see Display 7. Bookmark & Link Auditor: Scan to Load Bookmarks)

Display 7. Bookmark & Link Auditor: Scan to Load Bookmarks



3. Next, run Audit. Bookmarks with missing destinations, invalid page references, or structural hierarchy issues will fail validation and appear in the audit results for correction. (See Display 8. Bookmark & Link Auditor: Audit Results and Validation Status)

Display 8. Bookmark & Link Auditor: Audit Results and Validation Status



4. Review and resolve any issues identified by the audit.
5. Manually spot check bookmarks that point to critical CRF sections, such as:
    - Informed consent
    - Key efficacy assessments
    - Safety related forms
6. Save the final CRF PDF once QC is complete.

After QC, the CRF is ready for inclusion in the regulatory submission. Because the bookmark structure is defined in Excel, the same template can be reused or easily updated if page numbers or CRF content change.

RESULTS

Implementing this workflow, statistical programmers can:

- Reduce manual effort: Bookmarking time for large CRFs drops from hours to minutes.
- Increase accuracy: Excel-based editing minimizes human error and supports batch updates.
- Enhance reproducibility: Templates can be reused across similar documents or studies.
- Support compliance: The workflow aligns with regulatory requirements for bookmark structure, naming, and navigation.

DISCUSSION

For statistical programmers, automating CRF bookmarking is a game-changer. The manual process is not only tedious but also diverts valuable time from higher-level programming and QC tasks. By adopting the TRS toolbox workflow:

- Laborious tasks become streamlined.
- Standardization ensures consistency across submissions.
- Scalability supports single documents and large batches alike.
- Transparency provides a clear, auditable record of bookmark structures.

CONCLUSION

Automating CRF bookmarking using the TRS toolbox's import/export functionality and Excel templates offers significant efficiency and quality gains for statistical programmers. This workflow is scalable, reproducible, and supports compliance with regulatory requirements. Adoption of this approach can streamline submission preparation, reduce errors, and free programmers to focus on higher-value tasks.

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