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# Annotating PDFs using Adobe Reader X

Version 1.1 October 24, 2011

## 1. Know your version

The screen images in this document were captured on a Windows PC running Adobe Reader X. Though some of the images may differ in appearance from your platform/version, basic functionality remains similar. At the time of this writing, Adobe Reader X v10.1 is freely available and can be downloaded from: <http://www.adobe.com/products/acrobat/readstep2.html>

If you are running an earlier version of Adobe Reader, [click here](#).  
If you don't know your version of Adobe Reader, [click here](#).

## 2. What are eProofs?

eProof files are self-contained PDF documents for viewing on-screen and for printing. They contain all appropriate formatting and fonts to ensure correct rendering on-screen and when printing hardcopy. DJS sends eProofs that can be viewed, annotated, and printed using the free version of Acrobat Reader 7 (or greater). These eProofs are "enabled" with commenting rights, therefore they can be modified by using special markup tools in Acrobat Reader that are not normally available unless using the Standard or Professional version.

## 3. Comment & Markup toolbar functionality

### A. Show the Comment & Markup toolbar

The Comment & Markup toolbar doesn't appear by default. Do one of the following:

- Select View > Comment > Annotations.
- Click the Comment button in the Task toolbar.

*Note: If you've tried these steps and the Annotation Tools do not appear, your PDF may not be enabled for commenting.*

Contact [workflow\\_support.djs@sheridan.com](mailto:workflow_support.djs@sheridan.com) to resolve this issue.

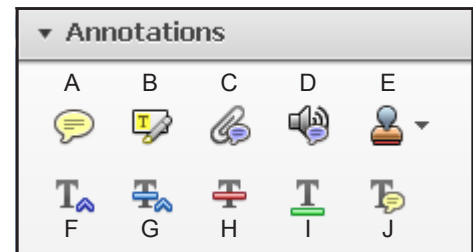
### B. Select a commenting or markup tool from the Annotations window.

*Note: After an initial comment is made, the tool changes back to the Select tool so that the comment can be moved, resized, or edited. (The Pencil, Highlight Text, and Line tools stay selected.)*

### C. Keep a commenting tool selected

Multiple comments can be added without reselecting the tool. Select the tool to use (but don't use it yet).

- Right Click on the tool.
- Select Keep Tool Selected.



- A. Sticky Note tool
- B. Highlight Text tool
- C. Attach File tool
- D. Record Audio tool
- E. Stamp Tool
- F. Insert Text tool
- G. Replace Text tool
- H. Strikethrough Text tool
- I. Underline Text tool
- J. Add Note to Text tool

## 4. The Properties bar


The Properties bar can be used to format text and select options for individual tools.

To view the Properties bar, do one of the following:

- Right-click the toolbar area; choose Properties Bar.
- Select [Ctrl-E]



## 5. Using the comment and markup tools

To *insert*, *delete*, or *replace* text, use the corresponding tool. Select the tool, then select the text with the cursor (or simply position it) and begin typing. A pop-up note will appear based upon the modification (e.g., inserted text, replacement text, etc.). Use the Properties bar to format text in pop-up notes. A pop-up note can be minimized by selecting the  button inside it.

editorial

# Still another activity by the highly promiscuous enzyme CYP3A4: 25-hydroxylation of cholesterol<sup>1</sup>

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8/24/2011 4:21:07 PM  
 Please note that this article exists for test purposes *only*.

8/24/2011 4:04:03 PM  
 put some awesome text here

8/24/2011 4:20:29 PM  
 text in comment boxes can be colored; you can also change the color of the box itself

8/24/2011 4:04:10 PM

is the most widely biochemical experiment of various biological systems against sterols. The levels of 25OHC are very low in the circulation and cells, however the physiological importance of this specific oxysterol is still uncertain. The possibility has been discussed that it may have a role in inflammation, and activation of the Toll-like receptors in macrophages induces formation of this oxysterol and its appearance in the circulation.

The origin of the 25OHC is likely to be mixed. A specific dioxygenase that converts cholesterol into 25OHC has been identified in a broad tissue distribution (3). In comparison with mice, the expression of this enzyme is very low in human tissues (3).

Under in vitro conditions, both CYP27A1 and CYP46A1 catalyze conversion of cholesterol into 25OHC in parallel with the major products 27-hydroxycholesterol and 24S-hydroxycholesterol, respectively (4, 5). In addition, 25OHC may be formed from cholesterol (6).

According to the data presented in this issue of the journal, 25OHC is present in the human circulation. Cells overexpressing human CYP3A4 have a significant stimulation of cholesterol oxidation caused an accumulation of cholesterol. Stimulation of CYP3A4 caused an accumulation of cholesterol from mouse liver.

troleanomycin, a specific inhibitor of CYP3A/Cyp3a, reduced the 25-hydroxylase activity. Finally, 25OHC levels in human sera correlated positively with levels of 4β-hydroxycholesterol (4OHC). The latter oxysterol is a well-established

in the same steroid structure. It has previously been shown that CYP3A4 is able to catalyze 25-hydroxylation of vitamin D, 1α-hydroxyvitamin D, and 5β-cholestane-3α,7α,12α-triol (9, 10). It is noteworthy, however, that a previous attempt to demonstrate 25-hydroxylase activity toward cholesterol by recombinant CYP3A4 failed (9). This study was not designed for studies on conversion of endogenous cholesterol into 25OHC, however, and a small conversion of added exogenous radioactively labeled cholesterol has been diluted with endogenous cholesterol and is difficult to detect.

The broad substrate specificity of CYP3A4 and the ability of this enzyme to hydroxylate a substrate molecule in several positions is likely to be due to the presence of more than one mode of binding and a unique flexibility of the active site. It has been shown that there is a dramatic conformational change upon binding of some substrates to this enzyme with an increase in the active site volume by 80% (11).

In one study on the rate of 24- and 25-hydroxylation of 1α-hydroxyvitamin D, there was a distinct difference in kinetics with 1α-hydroxyvitamin D<sub>2</sub> as substrate but not with 1α-hydroxyvitamin D<sub>3</sub> as substrate (10). Some residues at the active site of CYP3A4 important for modulation of the 24- and 25-hydroxylase activity were defined. At the present state of knowledge, it is not possible to evaluate if the same residues are of importance in connection with 25-hydroxylation of cholesterol.

A logical consequence of the fact that cholesterol is a substrate for CYP3A4 is that it may function as an inhibitor of the enzyme's activity. In accordance with this, Shinkyō and Guengerich (12) very recently reported that increasing levels of cholesterol in liver microsomes and in recon-

- A. Sticky Note
- B. Attached file
- C. Highlighted text
- D. Inserted text
- E. Crossed-out (strike-through) text
- F. Replaced text

## 6. Inserting symbols or special characters

An 'insert symbol' feature is not available for annotations, and copying/pasting symbols or non-keyboard characters from Microsoft Word does not always work. Use angle brackets < > to indicate these special characters (e.g., <alpha>, <beta>).

## 7. Editing near watermarks and hyperlinked text

eProof documents often contain watermarks and/or hyperlinked text. Selecting characters near these items can be difficult using the mouse alone. To edit an eProof which contains text in these areas, do the following:

- Without selecting the watermark or hyperlink, place the cursor near the area for editing.
- Use the arrow keys to move the cursor beside the text to be edited.
- Hold down the shift key while simultaneously using arrow keys to select the block of text, if necessary.
- Insert, replace, or delete text, as needed.

## 8. Summary of main functions

Insert text - Use Insert Text tool (position cursor and begin typing)

Replace text - Use Replace Text tool (select text and begin typing)

Delete text - Use Strikethrough Text tool (select text and press delete key)

Highlight text - Use Highlight Text tool (select text)

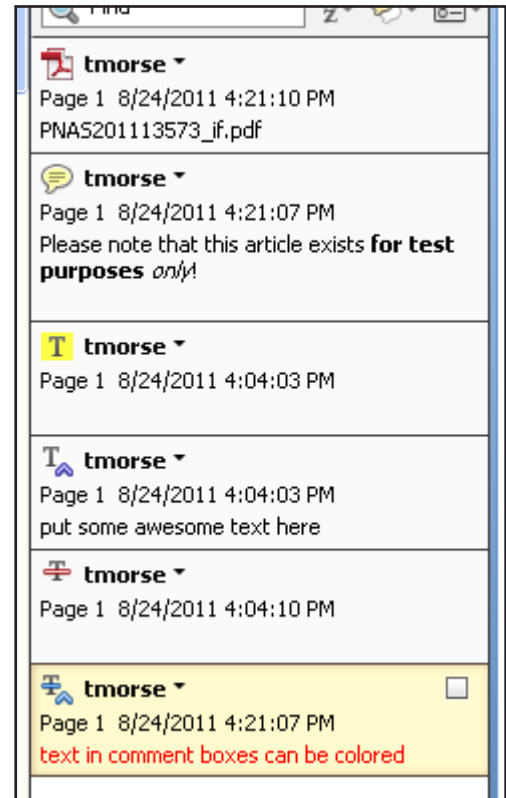
Attach a file - Use the Attach a File with Comment tool (select tool, position cursor and click mouse, select file)

## 9. Reviewing changes

To review all changes, do the following:

- Click the Comments button to reveal the comment tools
- Click the triangle next to Comments List (if not already visible)

Note: *Selecting a correction in the list will highlight the corresponding item in the document, and vice versa.*



Use the Comments list to review all changes