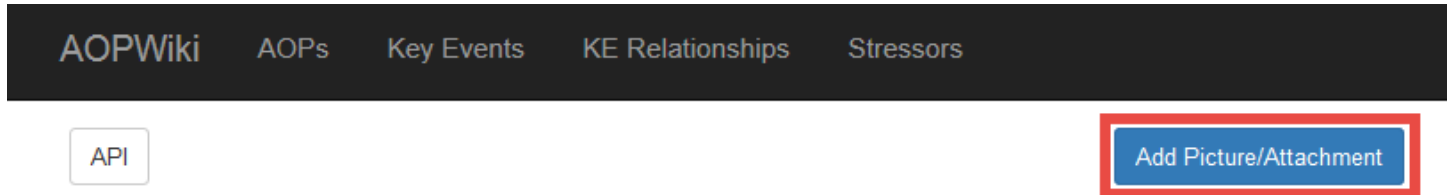


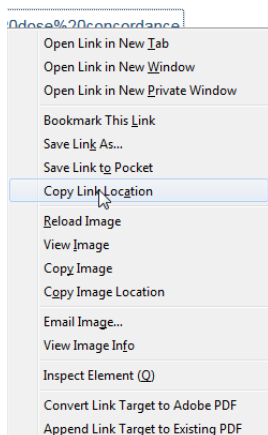
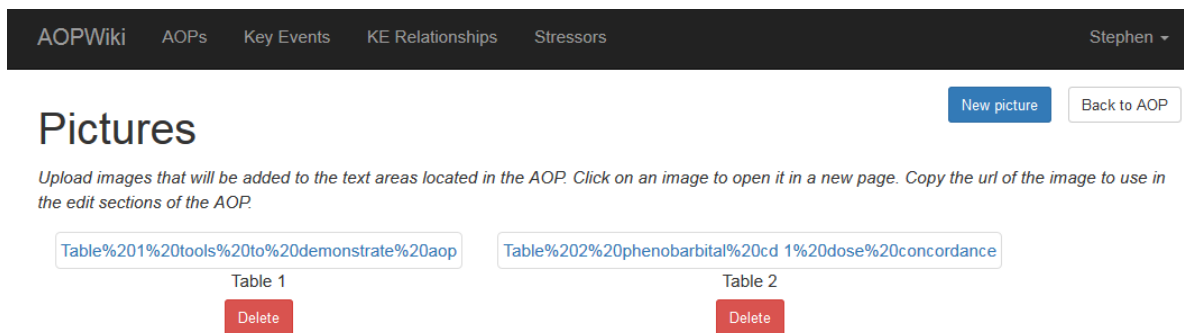
The formatting toolbar at the top of each text edit field includes icons for inserting either a link to a file or embedding an image (see below).



To use these tools, however, you must first upload the file to the server (unless the file is already available on the web). In order to do this, you need to click on the "Add pictures" button at the top of the page (Shown below for an AOP page).



On the subsequent page, you will click on the button labelled "New picture" at the top of the page and upload the desired file from your local computer. The Image Title should contain a short but informative label for your file. This is particularly important for non-image files because the content will not be displayed on the page listing the files. Once you've uploaded the desired file, right click on the file when looking at the list of all files for that AOP/KE/Relationship and select the "Copy link location" or "Copy image location" depending on the type of file you uploaded (see below for an example of a PDF file). Note that the wording may be slightly different depending on the operating system and browser that you are using.



After you have copied the link for the desired file, return to the AOP/KE/Relationship edit page insert your file link. The process is slightly different for an image vs. a file. To insert a link to a file, type the text you wish to display for the link. In the example below, "Table 2" was typed into the appropriate location in the edit box. Highlight the text you just typed and click the "Link" icon in the formatting bar as shown above. In the dialog box that opens, paste the link you copied in the previous step. Advanced options are available but not necessary. Simply click OK unless you wish to set additional settings. When you click the "Update AOP" button, you will now have a hyperlink associated with the text you entered at the appropriate place in your text field.

Phenobarbital causes an increase in the incidence of liver foci/tumors via the CAR activation AOP in male and female mice, and in certain strains of male and female rats (reviewed in Elcombe et al., 2014). For illustration, Table 2 shows the dose-response and time concordance of liver tumor incidence with phenobarbital exposure in male CD-1 mice. In this sex/strain, phenobarbital treatment for 2 years in the diet produced increased incidence of tumors at 75 and 150 mg/kg/day and no increase in tumor incidence at 10 mg/kg/day (Whysner et al., 1996). As shown in Table 2, a very strong dose concordance was observed for each KE or AE (as markers for in vivo CAR activation), with all of these events showing responses at the tumorigenic dose levels of 75 – 150 mg/kg/day. Certain early KEs or AEs produced effects at non-tumorigenic levels of 1.5 – 15 mg/kg/day, with increased PROD activity, a marker of CYP2B enzyme activity, being the most sensitive overall endpoint in male mice (Geter et al., 2014).

[Table 2](#)

Table 3 provides dose-response data for administration of phenobarbital in male mice of the C57BL/10J strain. A

When inserting an image, you do not need to type any text. Just place your cursor at the desired location in the text box and click the "Image" link in the formatting bar as shown above. In the dialog box that opens, paste the link to the image file you uploaded in the earlier step. The inserted image will now shown on the web page itself. This dialog box also has additional options should you wish to set them, but you can just click OK once you've pasted the link.