Improving drug safety decisions with more comprehensive searches
Example 1: Looking for additional indications beyond intended use of approved drug

A pharmaceutical company is conducting preclinical testing on a drug candidate that is similar to Ezogabine, an antiepileptic drug that targets potassium channels. Their drug is being developed to treat epilepsy and experimental data suggest that it affects smooth muscles, an area they have been exploring as an additional indication. They want to find out what information, if any, was presented in the approval package on Ezogabine effects on smooth muscle cells in order to provide support for ongoing studies and, or, to provide insights into potential risks (adverse events) that may be seen in their clinical trials.

Using the “Quick Search” bar in PharmaPendium, type in “Ezogabine smooth muscle cells”.

Of the fourteen results, line 6 provided insights on experimental findings regarding smooth muscle effects.
The Pharmacology Review discusses the effect of Ezogabine in a dog and pig study where the following observation was noted: "decrease in blood pressure was not accompanied by the expected reflex tachycardia which may indicate other nonvascular effects such as on the heart or its nervous system regulation." This finding suggests that potential adverse effects of the heart may be minimal and is consistent with their in vitro data. This finding also informs them of which non-rodent model system to potentially use.

Now they explore the new link “Search in Embase” to see if additional information has been published in the literature on Ezogabine and smooth muscle effects. Using this link, users can see if there is any additional information on potential adverse effects or if there is any insight into new indications.

The results in Embase will open in a new window with the same text query that was used in PharmaPendium. Sixteen results are retrieved that reference Ezogabine and smooth muscle cells.
Some interesting findings suggest that Ezogabine could be useful in treating other potential disorders. For example, result #2 suggests that Ezogabine could be an effective treatment for asthma when used in combination with Formoterol. Result #6 suggests that Ezogabine could play a role in treating periadventitial (the membrane surrounding organs and blood vessels) vasoregulation and associated hypertension.

These literature findings, combined with the findings from PharmaPendium, may be useful to help optimize preclinical and clinical study designs for the new drug candidate.

With this new functionality users have access to both precedent information and data from recently published preclinical/clinical models that could be used to test for new therapeutic indications and to help identify and develop mitigate plans for any unexpected adverse effects.
Example 2: Finding regulatory and literature evidence in a one session.

A company is interested in finding post-market published information on Tafluprost, a drug in the same class as one of the company's drug candidates that is entering clinical trials. This information could offer additional insights into potential testing that may be required during clinical development.

A “Quick Search” in PharmaPendium using the drug name followed by the term “post-marketing” found 18 entries.

The first entry contains a table summarizing all the on-going studies, including any Phase IV commitments. This investigator is specifically interested in looking at what Phase IV studies were required for Japanese or Asian patients at the time of drug approval. The study highlighted below is of particular interest: a significantly large study that will be conducted over the course of 2 years.
The abstract indicates that Tafluprost provided greater efficacy than the two other drugs, latanoprost and travoprost, over a 2 month period in a study group of Japanese. As the study is over a 2 year period, information on long term use will emerge.

Being better informed on the post-marketing requirements, as well as seeing some early stage results on the study, can help the company better understand how to mitigate any potential safety risks/concerns which impacts REMS planning and potentially their clinical trial designs for specific patient populations.

For more information please visit, www.elsevier.com/pharmapendium or www.elsevier.com/embase