Introduction: The FDA has limited options when faced with detecting emerging safety signals. A powerful new tool, the Janus Clinical Trials Repository (CTR) enables analysis of emerging signals in clinical trials and supports a more informed regulatory decision-making process. Specifically, the CTR is a modern data warehouse application that automatically processes and maintains a database of structured, standardized study data, and makes it available for reviewer access through a variety of analytical tools. Conceptually, the CTR will allow us to create databases easily to support meta-analyses of clinical trial data so that reviewers can focus on analyzing the data instead of spending time in preparing the datasets for analysis. The CTR is currently in development and only houses legacy diabetes data that CDER has converted under an ARRA PCOR-funded contract.

Methods: A proof-of-concept analysis was conducted by a group within CDER to demonstrate the value of the CTR’s ability to integrate standardized study data so that reviewers could analyze risk and safety signals across multiple studies. This analysis assessed the risk of bladder cancer and fractures with use of pioglitazone across multiple randomized studies and protocols. The originally submitted data had been converted into a standard format and loaded into the database. Analysis datasets were then built and analyzed using both SAS and JReview. These methods are exploratory and not meant to be robust from a meta-analysis methods perspective.

Results: Incidence of bladder cancer and fractures associated with pioglitazone use have been investigated in other large population trials and the results published in peer-reviewed literature. Performing this analysis using the CTR enabled reviewers to obtain similar results in a matter of days and with relative ease (as opposed to several months), positively demonstrating the potential value of the CTR in the detection of emerging signals. Our results were aligned with what has been published in the literature. The figures shown here are just some of our results.

Discussion: Compared to the time and expense of large-scale, epidemiological trials, we were able to approximate similar results in hours – with no additional participant burden or expense.

Conclusion: The CTR’s ability to store and manipulate standardized study data offers a variety of opportunities to enhance the regulatory decision-making process.