

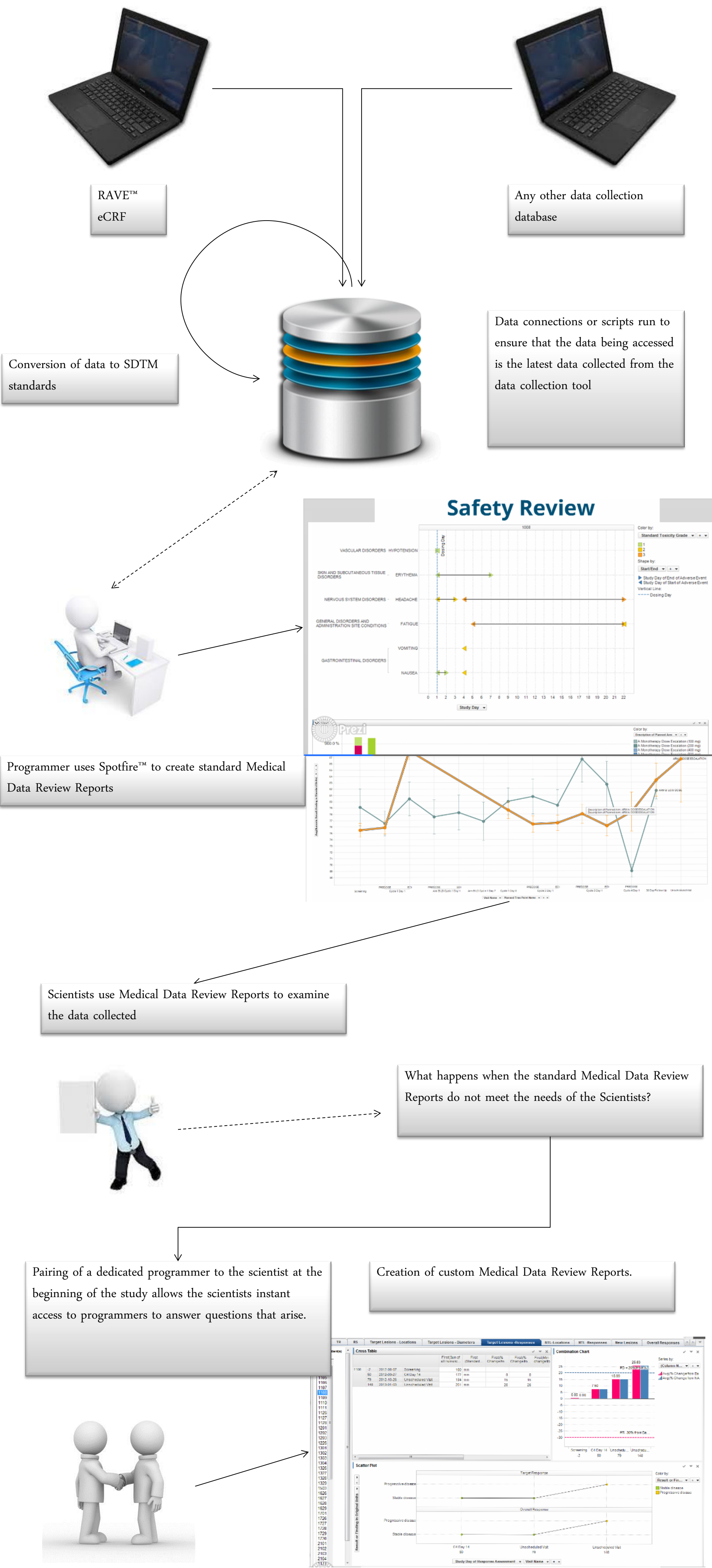
Medical Data Review and Exploratory Data Analysis using Data Visualization^(PP09)



Joel Allen

Data Provision Specialist
Clinical Data & Information Sciences, Roche Innovation Center Basel

1. Overview of the Process



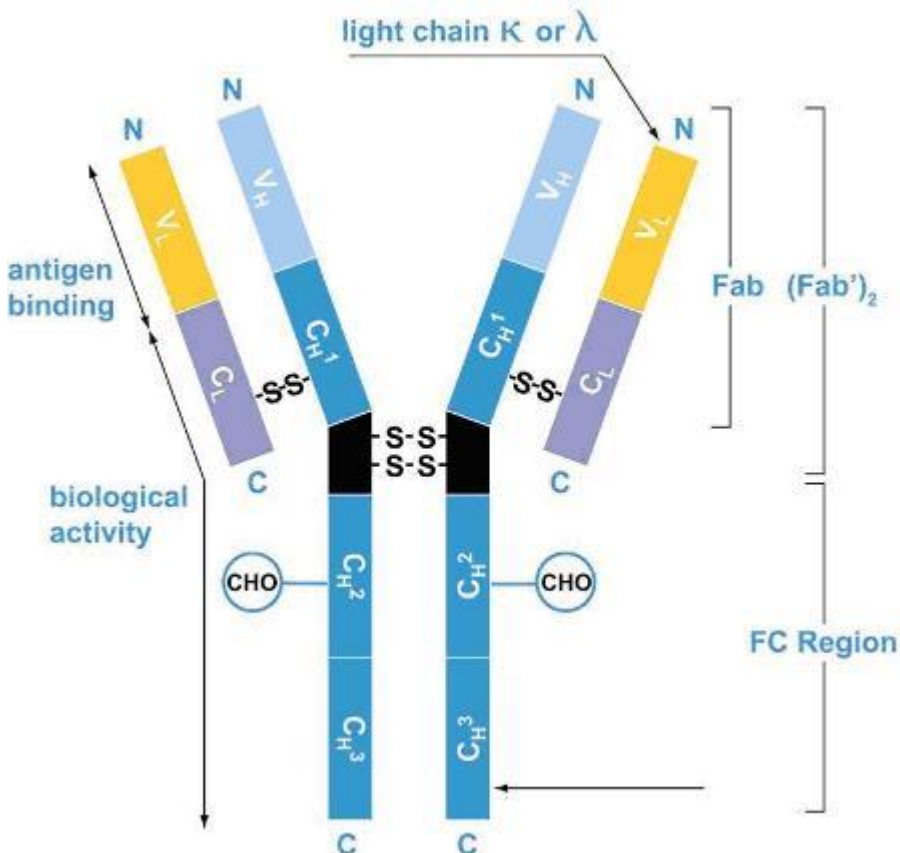
By having tools in place which will allow real time access to the data and programmers in place to collaborate with scientists, it allows real world problems to be solved in minutes or hours instead of days or weeks. A dedicated programming team exclusively catering to the scientific needs of a study teams requests, can greatly enhance the quality and quantity of the data that needs to be examined. Programming teams learn the requests of the scientific teams and modify the standard reports to enhance the usability of the Medical Data Review Reports. Scientific teams benefit from increased speed of outputs and an increase in quality of Reports.

2. The Example Problem

We observed increased levels of afucosylation in Lot X. Is there an increase of Adverse Events in Lot X as compared to the other Lots?

Background

Here we have a recombinant, humanized monoclonal antibody that is used to treat in an oncology study. Below is an example of a monoclonal antibody.



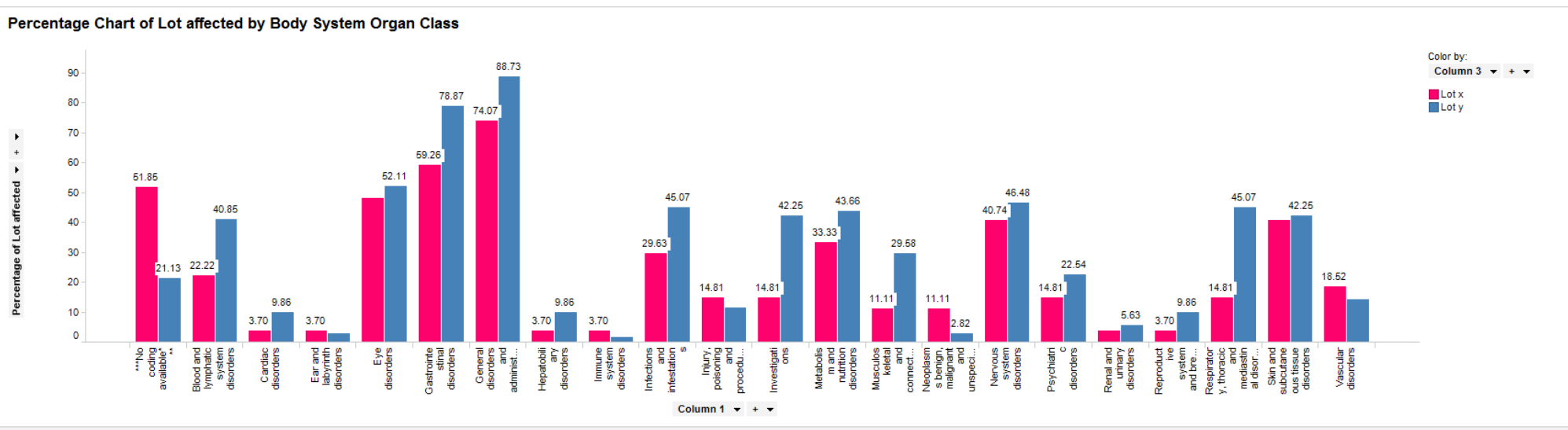
Where the Fab' region and the Fab' region bind to receptors on tumor cells and the FC region interact with the macrophages (are a type of white blood cell that engulf and digest cellular debris, foreign substances, microbes and cancer cells in a process called phagocytosis). Fucosylation is the process of adding fructose sugar units to a molecule, and hence afucosylation is the process of removing these sugar units to the molecule. These sugar molecules are typically found on the FC region of the monoclonal antibodies and have an effect on the interactions with the macrophages. Removal of core fucose selectively leads to enhanced cellular immune effector functions, being an increase of the interaction with the macrophages. Glycoengineering a monoclonal antibody is to remove the glycogens from the FC region of the monoclonal antibody to increase interactions with the macrophages.

Off-target toxicities, such as infusion-related reactions, are among the common adverse reactions of monoclonal antibodies. The vast majority of infusion reactions appear to be the result of antibody-antigen interactions resulting in cytokine release. The efficacy and safety of antibodies with enhanced effector functions are challenging to assess preclinically because of differences in the immune systems across species. Based on extensive preclinical and clinical experience with monoclonal antibodies, there is no clear evidence supporting an association between afucosylation and non-specific off-target toxicities, such as infusion-related reactions.

So this recombinant, humanized monoclonal antibody was **not** glycoengineered to increase macrophage activity, so hence was the naturally occurring Lot X afucosylation of our monoclonal antibody a cause for concern?

3. The Solution

By using Spotfire™, we could quickly discover which patients had taken Lot X and the corresponding Adverse Events associated with that Lot. As you can see in the bar graph below, very few of the Lot X patients experienced more Adverse Events then the rest of the Lots in any of the Body System Organ Classes coded.



4.CONCLUSION

Although the above description of the problem is not unique, in conjunction with the process described, it allows for quick and accurate resolution of the problem. By pairing scientific experts with computer programmers, we allow for quick and accurate information to be disseminated to a large group of people quickly. Having these types of problems answered quickly and accurately, it allows us to save time ,money, and improve patients lives. Doing now what patients need next.

We at pRED have created a powerful data visualization interface allowing quick, accurate and high quality data evaluation, incorporating eCRF, numerical, electronic and graphical data with the medical images to provide optimum data value for each study.

