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Fusarium Head Blight (FHB) continues to be a concern in many wheat and barley production regions of the world. Through collaborative research funded by the USWBSI, Web-based risk assessment models were developed and deployed in 2004 to provide timely predictions of FHB risk in 23 states. Missing from these models, however, is a direct prediction of the risk of DON accumulation. Current goals of the cooperative epidemiology group include adding a DON module for existing models and developing mechanistic models for FHB and DON in wheat and barley. These goals are consistent with research priorities of the EEDF RAC. Experiments proposed herein will address these goals and priorities. The specific objectives are: **i)** determine the influence of environment and variety resistance on the probability of infection and DON accumulation and **ii)** determine the effects of fungicide application, variety resistance, and disease variability on the relationship between FHB index (IND) and DON, and characterize the “tolerance” of common wheat varieties to DON accumulation. Two sets of field experiments will be conducted. In the first, a standard protocol will be used by the epidemiology group to conduct experiments at ND, SD, PA, NE, and OH. The experimental design will be a split-split plot, with 3 replicate blocks. Two planting dates will serve as the whole plot factor; wheat varieties with similar maturity and different levels of resistance to FHB (“Cooper”, susceptible; “Hopewell”, moderately susceptible; and “Truman”, moderately resistant) as the sub plot factor; and inoculation timing (no inoculation, inoculation at early flowering, and inoculation at mid flowering) as the sub-sub plot factor. Sub-sub plots will be spray-inoculated with a spore suspension of *Fusarium graminearum* either at early anthesis (Feekes’ GS 10.5.1), mid anthesis (GS 10.5.5) or left un-inoculated. In the second experiment, field plots will be planted with six soft red winter wheat varieties (“Cooper” and “Pioneer 25R47”, susceptible to FHB; “AG101” and “Hopewell”, moderately susceptible to FHB; and “Truman” and “McCormick”, moderately resistant) in a split plot experimental design, with 3 replicate blocks. Variety and fungicide will serve as the whole- and sub-plot factors, respectively. Each whole plot will be divided into three sub-plots; one will be left untreated, one treated with Folicur, and the third treated with Prosaro at GS 10.5.1. FHB intensity will be assessed and grain DON content analyzed in both experiments. Models will be developed to estimate the probability of infection and DON exceeding critical threshold levels, given weather conditions at the time of infection and variety susceptibility. In experiment two, spikes in specific disease categories and clusters within plots will be tagged, harvested, and analyzed for DON. We will quantify the effects of IND variability, variety susceptibility, and fungicide on the IND/DON relationship at the individual spike and plot levels. Understanding the influence to IND variability on this relationship will help us to develop sampling protocols to improve pre-harvest estimates of DON from IND. Information gathered through this and related studies will be used to advance modeling efforts.