eAppendix

The following code is the generic specification of an unconstrained logistic regression model with a non-informative prior on parameters beta1 and beta2. X and Y indicate exposures of interest as specified in our example (or in a given dataset).

```
proc mcmc data=MCMC nmc=*Input number of iterations* nbi=*Input number of burn-in* monitor=(beta0 beta1 beta2) /*SEED =________*/;

parms (beta0 beta1 beta2) 0; *this indicates starting values for the simulation;

prior beta0 beta1~normal(0, var=1e6);
prior beta2 ~ normal(0, var=1e6);

p = logistic(beta0 + beta1*X +beta2*Y);

model case ~ binomial(n,p);

run;
```

The following code is an adaptation of the code above with integration of an order constrained prior for exposure Y relative to X. In this scenario, we specify a prior, as in our example, that beta2 is greater than or equal to beta1. A non-informative prior is retained for beta1. In the absence of data, this prior is centered at a median value of 1.00 (90% HPD: -6.00, 7.00). This can be illustrated if the user simply removes ‘X’ and ‘Y’ from the model ‘p’. This code can be adapted to include order constraints for multiple exposures of interest, or categories of a single exposure as in dose-response analyses.

```
proc mcmc data=MCMC nmc=*Input number of iterations* nbi=*Input number of burn-in* monitor=(beta0 beta1 beta2) /*SEED =________*/;

parms (beta0 beta1) 0;

prior beta0 beta1~normal(0, var=1e6);
prior beta2 ~ normal(0, var=1e6, lower=beta1, upper=1e6);

p = logistic(beta0 + beta1*X +beta2*Y);

model case ~ binomial(n,p);

run;
```

Simulation: We present three different scenarios where (1) the order constraint does not change parameter estimates, (2) the order constraint biases parameter estimates, and (3) where the order constraint improves the estimates of a weak parameter relative to a well-identified parameter. Simulation 1 and 2 specify x1 and x2 as Bernoulli with probability 0.5. In simulation 3, we specify x1 and x2 as Bernoulli with probability 0.5 and 0.05, respectively. All simulations were repeated 100 times. The final scenario is similar to that seen in the example of the Savannah River Site cohort exposed to gamma and beta radiation from tritium; the effect of β_1 is well identified from the data but there is substantially less information regarding the effect of β_2. We measure the change in estimates with MSE. Simulation 1 shows no change in MSE using an order constraint while simulation 2 shows an increase in MSE associated with an order constraint that biases parameter estimates. In simulation 3, the MSE indicates that when the data for one variable (x2) are weaker than a reference variable (x1), the order constraint will be closer to the true value, on average.

			Parameter estimates					
			β_1			β_2		
			mean	std dev	MSE	mean	std dev	MSE
Simulation	True Values	N						
1	β_1=1, β_2=2	1,000						
	no constraint		0.998	0.142	0.020	2.01	0.158	0.025
	$\beta_2 \geq \beta_1$		0.998	0.141	0.020	2.01	0.158	0.025
2	β_1=1, β_2=0	1,000						
	no constraint		1.00	0.162	0.026	0.004	0.163	0.027
	$\beta_2 \geq \beta_1$		0.672	0.134	0.126	0.728	0.132	0.547
3	β_1=1, β_2=2	500						
	no constraint		0.993	0.234	0.055	2.08	0.460	0.218
	$\beta_2 \geq \beta_1$		0.995	0.234	0.055	2.14	0.400	0.180