



September 20, 2007

## CENTER FOR VETERINARY BIOLOGICS NOTICE 07-15

United States  
Department of  
Agriculture

Animal and Plant  
Health Inspection  
Service

Veterinary Services

Center for Veterinary  
Biologics

510 S. 17<sup>th</sup> Street  
Suite 104  
Ames, IA 50010

(515) 232-5785  
FAX (515) 232-7120

Subject: Software Patch for Estimating Prevented Fraction Confidence Intervals

To: VS Management Team (VSMT)  
Directors, Center for Veterinary Biologics  
Biologics Licensees, Permittees, and Applicants

### I. PURPOSE

This notice is to alert users to an available patch for a commercial statistical software package.

### II. BACKGROUND

The prevented fraction is the complement of the risk ratio:  $PF = 1 - p_v / p_c$ , where  $p_v$  and  $p_c$  are the affected fractions of vaccinates and controls, respectively. Interval estimates of  $PF$  may be obtained by taking the complement of an interval estimate of the risk ratio.

To estimate a confidence interval for the risk ratio, the Center for Veterinary Biologics (CVB) Biometrics Section typically uses the two one-sided score test (TOSST) procedure.<sup>1</sup> Asymptotic intervals based on the score statistic have been widely used.<sup>2,3,4</sup> The exact TOSST procedure is a computer-intensive method recommended for smaller sized studies. It utilizes the score statistic to define the tail area, and the tail area probability is then calculated by the binomial probability mass function.

<sup>1</sup> Agresti A, Min Y, 2001. On small-sample confidence intervals for parameters in discrete distribution. *Biometrics* 57: 963-971.

<sup>2</sup> Koopman PAR, 1984. Confidence intervals for the ratio of two binomial proportions. *Biometrics* 40: 513-517.

<sup>3</sup> Miettinen O, Nurminen M, 1985. Comparative analysis of two rates. *Statistics in Medicine* 4: 213-226.

<sup>4</sup> Gart JJ, Nam J, 1988. Approximate interval estimation of the ratio of binomial parameters: a review and correction for skewness. *Biometrics* 44: 323-338.



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### III. GUIDANCE

The TOSST method is implemented in the commercial software package StatXact. The two versions<sup>5</sup> of StatXact are represented as identical except for the user interface. The CVB recently became aware that the two versions have been producing discrepant results for risk ratio confidence intervals by the TOSST method. Independent calculations by the CVB Biometrics Section in specific instances led us to conclude that the Windows version appeared to give the correct estimates. The software vendor, Cytel Inc., notified us today that a patch for the PROCs version has been made available at <http://www.cytel.com/Support/psx7patch.asp>. Licensees using the PROCs version of StatXact are advised to implement the patch.

/s/Richard E. Hill, Jr.

Richard E. Hill, Jr.  
Director  
Center for Veterinary Biologics

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<sup>5</sup> StatXact 7 for Windows with patch and StatXact 7 PROCs, Cytel Inc.