TABLE 3.3
Estimates of p_2 for Various Choices of δ

				$\hat{p}_2$			
x_0	$\hat{y}$	ν	ν'	δ = 0.05	δ = 0.01	δ = 0.02	δ = 0.5
1.0	1.147	8	2	0.064	0.129	0.258	0.616
5.2	8.921	259	93	0.441	0.757	0.977	1.000

on the corresponding clinical outcome can be assessed by means of the closeness of the predicted value and the observed response in terms of either criterion based on absolute change or relative change. The degree of criticality risk ranking can be determined based on some prespecified p_0. For example, if p is larger than 80%, we may assign the CQA to Tier 1; if p is within 60% and 80%, we may consider that the CQA is mild to moderate relevant to clinical outcome and hence the quality attribute should be assigned to Tier 2. Those quality attributes whose p values are <60% will be assigned to Tier 3, which is least relevant to clinical outcome.

The above process for the development of the predictive model is usually referred to as a *one-way translational process* in translational research/medicine. That is, the information observed at basic research discoveries is translated to the clinic. As indicated by Pizzo (2006), the translational process should be a *two-way translational process*. In other words, we can exchange x and y in Equation 3.1

$$x = \gamma_0 + \gamma_1 y + \varepsilon$$

and come up with another predictive model $\hat{x} = \hat{\gamma}_0 + \hat{\gamma}_1 y$. The idea for the validation of a two-way translational process can be summarized by the following steps:

Step 1: For a given set of data (x, y), establish a predictive model, say, $y = f(x)$.

Step 2: Evaluate $\hat{p}_1 = P\{|y - \hat{y}| < \delta_1\}$ and assess the one-way closeness between y and $\hat{y}$ based on a test for hypotheses 3.3. Proceed to the next step if the one-way translation process is validated.

Step 3: Consider x as dependent variable and y as independent variable and set up the regression model. Predict x at the selected observation y_0, denoted by $\hat{x}$, based on the established model between x and y (i.e., $x = g(y)$). Note that in the above example,

$$\hat{x} = g(y) = \hat{\gamma}_0 + \hat{\gamma}_1 y$$

Step 4: Evaluate the closeness between x and $\hat{x}$ based on a test for the following hypotheses

$$H_0 : p_1 \le p_0 \text{ versus } H_a : p_1 > p_0, \tag{3.4}$$

where $p_1 = P\{|x - \hat{x}| < \delta\}$.