Tsubota et al. (115) and De Rojas et al. (116) provide photographs of eye damage in SJS. FDA's Guidance for Industry documents relating to smallpox vaccines (117) and lamotrigine (118) also specifically warn against SJS.

g. Using raw data on adverse events to acquire cause-and-effect data on adverse drug reactions

The Naranjo questionnaire consists of ten questions that capture information regarding any given AE (119,120,121,122). These questions are shown below:

1. Are there previous conclusive reports on this reaction?
2. Did the adverse event appear after the suspected drug was administered?
3. Did the adverse reaction improve when the drug was discontinued or a specific antagonist was administered?
4. Did the adverse reaction reappear when the drug was readministered?
5. Are there alternative causes (other than the drug) that could on their own have caused the reaction?
6. Did the reaction reappear when a placebo was given?
7. Was the drug detected in the blood (or other fluids) in concentrations known to be toxic?
8. Was the reaction more severe when the dose was increased or less severe when the dose was decreased?
9. Did the patient have a similar reaction to the same or similar drugs in any previous exposure?
10. Was the adverse event confirmed by any objective evidence?

This questionnaire includes factors such as prior adverse reports, the timing of the adverse reaction, whether the adverse reaction stopped when the drug was discontinued and whether it reappeared when the drug was resumed, dosage levels, and alternative causes of the AE (123). The questionnaire uses a point system, with assigned points being

[115] Tsubota K, Satake Y, Kaido M, et al. Treatment of severe ocular-surface disorders with corneal epithelial stem-cell transplantation. *N Engl J Med*. 1999;340:1697–1703.

[116] De Rojas MV, Dart JK, Saw VP. The natural history of Stevens Johnson syndrome: patterns of chronic ocular disease and the role of systemic immunosuppressive therapy. *Br J Ophthalmol*. 2007;91:1048–1053.

[117] U.S. Dept. of Health and Human Services. Food and Drug Administration. Guidance for Industry. Vaccinia virus developing drugs to mitigate complications from smallpox vaccination. March 2004 (40 pages).

[118] U.S. Dept. of Health and Human Services. Food and Drug Administration. Guidance for Industry. Nonclinical safety evaluation of pediatric drug products. February 2003 (22 pages).

[119] Naranjo CA, Busto U, Sellers EM, et al. A method for estimating the probability of adverse drug reactions. *Clin Pharmacol Ther*. 1981;30:239–245.

[120] van Jaarsveld CH, Jahangier ZN, Jacobs JW, et al. Toxicity of anti-rheumatic drugs in a randomized clinical trial of early rheumatoid arthritis. *Rheumatology (Oxford)*. 2000;39:1374–1382.

[121] Papastavros T, Dolovich LR, Holbrook A, Whitehead L, Loeb M. Adverse events associated with pyrazinamide and levofloxacin in the treatment of latent multidrug-resistant tuberculosis. *Can Med Assoc J*. 2002;167:131–136.

[122] Oberg KC. Adverse drug reactions. *Am J Pharm Educ*. 1999;63:199–204.

[123] Kami S. Kendall v. Hoffman-La Roche, Inc., et al., No. A-2633-08T3, N.J. Super. App.