



American Society for Quality ([www.asq.org](http://www.asq.org)) – Washington D.C. and Maryland Metro, Section 509 ([www.asq509.org](http://www.asq509.org))

**Biomed/Biotech Special Interest Group (SIG) Meeting**

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**“Root Cause Analysis and Corrective/Preventive Actions – Investigation of Curious Cloudiness in a Process Intermediate during Manufacturing of Meningococcal Vaccine”**

To be presented by

**Bob Kruse, PhD**

([drbobkruse@verizon.net](mailto:drbobkruse@verizon.net))

**Pharmaceutical Manufacturing Support Specialist**

**Wednesday, July 11, 2012**

6:00 – 6:20 PM – Networking; Pizza/drink

6:20 – 8:30 PM – Program

8:30 – 8:45 PM – Door-prizes drawing; Networking

**Online Registration site:** <http://www.asq509.org/ht/d/DoSurvey/i/35817>

**Open to Public –**

**\$5:** [non-ASQ members](#) to cover pizza/drink cost;

**Free:** [ASQ Members, veterans, senior citizens, students, local interns, residents, postdocs, FDA Commissioner’s Fellows, and current job-seekers](#)

**Location:** Kelly’s Deli Conference Center, 7519 Standish Place, Rockville, MD 20855

**Registration Deadline:** Please register by **Wednesday noon, July 11, 2012.**

**Question:** Please contact Dr. C.J. George Chang, Chair of Biomed/Biotech SIG, ASQ509; [gchang2008@yahoo.com](mailto:gchang2008@yahoo.com) or 240-793-8425 (cell).

**Driving directions:** **By Car:** From I-270 (N or S bound): Take Exit 9A and exit from the FIRST right exit; turn left (east) onto Shady Grove Dr.; turn right (south) onto Rockville Pike (**Route 355**); turn left (east) onto East Gude Dr.; turn left (north) immediately onto Crabb’s Branch Dr.; turn left (west) immediately onto Standish Place. The first building on your right side is 7519 Standish Place; open parking). [The venue is on the first floor with its entrance opposite to the left side of building main entrance.](#) **By Metro train:** Off from Red Line **Shady Grove Station**, and take RideOn **Route 59 TOWARD ROCKVILLE** and get off from “**Calhoun Place**” stop. Standish Place is next to the Bus stop. Our venue is within 2 min of walking distance from the stop.

## Summary: Investigation of Curious Cloudiness in a Process Intermediate during Manufacturing of Meningococcal Vaccine

*Neisseria meningitidis*, often referred to as **meningococcus**, is a bacterium that can cause meningitis and other forms of meningococcal disease such as meningococemia, a life threatening sepsis. *N. meningitidis* is a major cause of morbidity and mortality during childhood in industrialized countries. Approximately 2500 to 3500 cases of *N. meningitidis* infection occur annually in the United States, with a case rate of about 1 in 100,000. Children younger than 5 years are at greatest risk, followed by teenagers of high school ages.

For ten years, a **conjugate vaccine** against *N. meningitidis* strain C was episodically manufactured at one plant in US. The bacterial culture used was not genetically modified and fermentation parameters were unchanged over this period. Purification of the antigenic component and its subsequent conjugation processes were validated, stable based on chemical characterization of the product, and procedurally unchanged for more than one hundred production batches. In 2010, a mysterious precipitation suddenly appeared in one of the process intermediates. Experienced operators who had monitored the process from its development and through commercial manufacturing had never before seen this aberration. Production of the vaccine was halted for four months while the investigation proceeded and before corrective action could be implemented.

An overview of the manufacturing process will be presented, with emphasis on some unusual chemical modifications to the key antigen. The second half of the presentation will describe the direction of the investigation that lead to the identification of the cause of the precipitation and its corrective action.

### Presenter's Bio: Bob Kruse, PhD

Bob Kruse earned his B.Sc. in Biology from the University of Vermont in 1981, and a Ph.D. in Microbiology from Cornell University in 1988. He has worked in the pharmaceutical and biotechnology fields since then; at Armour Pharmaceuticals, American Home Products, and most recently, Baxter BioScience. He has also made two excursions into academia; teaching Biology at Gettysburg College in Pennsylvania and Mt. Mary College in Milwaukee.

Dr. Kruse's industrial positions have focused on process development, QC, Regulatory submissions, and technical support for manufacturing. He has led many investigations of out-of-specification (OOS) material to determine its root cause and to prescribe appropriate corrective and preventative actions.