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Masaru Shiratori
Genentech, shiratori.masaru@gene.com

Jessica Wuu
Genentech

Martin Gawlitzek
Genentech

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IDENTIFICATION OF CELL CULTURE LEVERS TO LOWER TRISULFIDE MODIFICATIONS IN MONOCLONAL ANTIBODIES PRODUCED IN CHO CELL CULTURE

Masaru Shiratori, Genentech, Inc.
shiratori.masaru@gene.com
Jessica Wuu, Genentech, Inc.
Martin Gawlitzek, Genentech, Inc.

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Trisulfide bond formations are a commonly observed modification of monoclonal antibodies produced in cell culture processes. Protein trisulfide bonds are post-translational modifications in which an extra sulfur atom is bound between two cysteines involved in disulfide bonding. This modification has been detected in both recombinant and endogenous plasma-derived IgGs. Inconsistent levels of trisulfides were identified as a source of variability observed during the conjugation process for antibody-drug conjugates (ADCs). To understand the root cause for variable trisulfide levels observed during process development for different molecule projects, cell culture studies aimed at identifying process levers to minimize trisulfide formation were conducted. Several cell culture factors, including different media components, were identified and tested to lower product trisulfides and minimize the variability at time of harvest. An assessment of concerns about product trisulfide levels will be presented. Finally, identified levers and potential mechanism(s) involved in product trisulfide formation during cell culture will be discussed in this presentation.