

We claim:

1. A liquid chromatography-free method for quantifying target antibodies in a sample comprising:
 - spiking the sample with a labeled internal standard antibody;
 - digesting the antibodies in the sample to produce peptides;
 - fractionating the peptides; and
 - quantifying the target antibodies using a direct infusion MS² system containing one or more ion traps and two or more quadrupole mass filters and an electrospray ionizer, wherein the method is liquid chromatography-free.
2. The method of claim 1, further comprising the step of spiking the peptides with labeled, tagged Fc peptide VSVLTVLHQDWLNGK (SEQ ID NO:1) prior to fractionation.
3. The method of claim 1 or 2, wherein the peptides are fractionated by solid phase extraction.
4. The method of claim 3, wherein the solid phase extraction is reverse phase solid phase extraction.
5. The method of any one of claims 1-4, wherein labeled internal standard antibody and the mass-tagged Fc peptide are labeled with a heavy isotope.
6. The method of claim 5, wherein the heavy isotope is selected from the group consisting of ¹³C, ¹⁵N, and ²H.
7. The method of any one of claims 1-6, wherein the target antibody is a human monoclonal antibody.
8. The method of any one of claims 1-7, wherein the mass spectrometry system is a tandem mass spectroscopy system.

9. A method of quantitating a protein drug product in a biological sample comprising:
spiking the sample with a known amount of a heavy mass tagged peptide standard having an amino acid sequence according to SEQ ID NO:1;
digesting protein drug product in the sample into peptides;
fractionating the peptides under conditions that retain peptides having an amino acid sequence according to SEQ ID NO:1;
analyzing the sample containing the protein drug product peptides and the peptide standards for the presence of the peptide having an amino acid sequence according to SEQ ID NO:1 using an MS² system to calibrate the system, wherein the MS² system comprises one or more ion traps and two or more quadrupole mass filters and an electrospray ionizer; and
quantitating the amount of protein drug product present in the sample based upon the presence of the peptide, wherein the method does not utilize liquid chromatography.
10. The method of claim 9, wherein the data for quantifying drug product ions and mass tagged peptide standard ions are acquired in different MS² scans.
11. The method of claim 9, wherein the peptides are fractionated using reverse phase solid phase extraction.
12. The method of claim 4 or 11, wherein the reverse phase solid phase extraction uses 15 to 25% acetonitrile as a wash and 20 to 30% acetonitrile elution.
13. The method of claim 9, further comprising spiking the sample of protein drug product with a heavy isotope-labeled protein drug product prior to digesting the sample.
14. The method of claims 1 or 9, wherein the protein drug product comprises an antibody or an antigen binding fragment thereof, a recombinant protein, a fusion protein, or a combination thereof.
15. The method of any one of claim 1-14, wherein the sample comprises serum.

16. The method of any one of claims 1-15, wherein the method has a dynamic range of 1 to 1000 $\mu\text{m}/\text{mL}$.
17. The method of any one of claims 1-16, wherein the method has Lower Limit of Quantification (LLOQ) of 1-2 $\mu\text{g}/\text{mL}$.
18. The method of any one of claims 1-17, wherein the method is an automated high throughput method.
19. The method of claim 18, wherein the method has an analytic speed of less than 1 minute per sample.