

What is claimed is:

1. A computer-implemented method of determining criticality of a product quality attribute (PQA) of an antibody after multiple administrations of the antibody to a subject, comprising:

(a) predicting an *in vivo* serum concentration of the antibody with a PQA after a single administration of the antibody by:

(i) predicting a percentage of the antibody with the PQA using an *in vivo* rate constant determined for the PQA, wherein an *in vivo* rate constant is determined by quantitating a percentage of the PQA as a function of time and fitting the quantitated percentage of the PQA to the equation $P_{PTM}(t) = 1 - (1 - P_0) \cdot e^{-k_{PTM}t}$, where $P_{PTM}(t)$ is the proportion of the PQA as a function of time; P_0 is an initial percentage post-translational modification; and k_{PTM} is the PQA rate constant; and

(ii) multiplying the predicted percentage of the antibody with the PQA by a total *in vivo* concentration of the antibody to determine the concentration of the antibody with the PQA and thereby producing a single-administration model;

(b) repeating step (a) at least once and thereby producing one or more additional single-administration models;

(c) superimposing the single-administration models of steps (a) and (b) and thereby producing a multiple-administration model; and

(d) using the multiple-administration model to determine the criticality of the PQA,

wherein the PQA includes a post-translational modification of interest.

2. The method of claim 1, further comprising determining the exposure of the subject to the antibody with the post-translational modification of interest, wherein determining an exposure of the subject to the antibody with the post-translational modification of interest comprises determining the area under the curve (AUC) of the concentration of the antibody with the post-translational modification of interest.

3. The method of any one of claims 1 or 2, wherein the serum concentration of

the antibody is described by a two-compartment pharmacokinetic model equation as $C(t) = Ae^{-\alpha t} + Be^{-\beta t}$, where A and B are hybrid coefficients when α and β are hybrid first order constants, respectively.

4. The method of any one of claims 1-3, wherein the antibody comprises a recombinant therapeutic monoclonal antibody.
5. The method of any one of claims 1-4, wherein the PQA can impact drug stability, safety, and/or efficacy.
6. The method of any one of claims 1-5, wherein the method is used to predict or monitor the post-translational modification profile of a monoclonal antibody.
7. The method of any one of claims 1-6, wherein the post-translational modification comprises one or more of deamidation, oxidation, glycation, disulfide formation, N-terminal pyroglutamate formation, C-terminal lysine removal, and high mannose glycosylation.
8. The method of any one of claims 1-7, further comprising modeling a correlation between pharmacokinetic concentration and proportion of post-translational modification variants.
9. The method of any one of claims 1-8, further comprising quantitatively assessing and predicting the subject exposure to a representative post-translational modification in either a single-dose regimen or a multiple-dose regimen.
10. The method of any one of claims 1-9, further comprising predicting a maximum and a minimum post-translational modification level observed in a multiple-dose regimen.
11. The method of any one of claims 1-10, further comprising determining a total *in vivo* concentration of the antibody in the subject.
12. The method of any one of claims 1-11, further comprising predicting a pre-dose *in vivo* concentration of an antibody with the post-translational modification of interest.

13. The method of any one of claims 1-12, further comprising predicting a post-dose *in vivo* concentration of an antibody with the post-translational modification of interest.