WO2013/006454 discloses arginine-free polypeptide-containing compositions wherein the arginine used in similar compositions as that disclosed in EP1478394 B1 has been replaced with salts, which according to the example provided is 140 mM (see example 1). No reference is made to stabilization at high temperatures. Indeed, the compositions disclosed therein are stored as a liquid at 2-8°C or frozen.

The present invention addresses these problems by providing a novel stable liquid formulation that allow storage of TNFR:Fc polypeptides. The inventors, surprisingly, have observed that stable aqueous compositions as disclosed herein can be prepared completely free of Arginine and Cysteine and are highly stable at high temperatures.

SUMMARY ~~OF THE INVENTION~~

~~FIRST ASPECT OF THE PRESENT INVENTION~~

The ~~first aspect of the~~ present ~~invention~~ disclosure is based on the finding that a certain amount of salt in an aqueous formulation comprising an isolated polypeptide that is an extracellular ligand-binding portion of a human p75 tumor necrosis factor receptor fused to the Fc region of a human IgG1, can result in an increase of stability of the protein at high temperatures, above 5 °C. Furthermore, the election of the salt concentration is such that it is close to the physiological body salt concentration.

Therefore, the present ~~invention~~ disclosure relates to an aqueous composition comprising:

- an isolated polypeptide that is an extracellular ligand-binding portion of a human p75 tumor necrosis factor receptor fused to the Fc region of a human IgG1;
- salt present at a concentration of from 80 to 130 mM; and
- an excipient selected from the group of trehalose and sucrose and combinations thereof,

characterized in that neither arginine nor cysteine are present in the composition.

In one aspect, there is provided an aqueous composition comprising: an isolated polypeptide that is an extracellular ligand-binding portion of a human p75 tumor necrosis factor receptor fused to the Fc region of a human IgG1; salt present at a concentration of from 80 to 130 mM; an aqueous buffer, wherein the aqueous buffer is sodium and/or potassium phosphate buffer and wherein the aqueous buffer is present at a concentration of 20 to 30 mM; and an excipient which is sucrose, wherein the concentration of sucrose is between 34-80 mg/mL, characterized in that neither arginine nor cysteine are present in the composition.

In one aspect, there is provided an aqueous composition comprising: an isolated polypeptide that is an extracellular ligand-binding portion of a human p75 tumor necrosis factor receptor fused to the Fc region of a human IgG1; salt present at a concentration of from 80 to 130 mM, wherein the salt is not present at a concentration of 100 mM; an aqueous buffer, wherein the aqueous buffer is succinate buffer; and an excipient selected from the group of trehalose and sucrose or a combination thereof, characterized in that no free amino acids are present in the composition.

BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1 shows a bar chart showing relative unfolding temperatures (T_{onset}/°C) found for all samples with error bars found using the fluorescence ratio between 330 and 310 nm.