whilst exposing the subjects to which the compositions are administered to a lower lipid and/or lower volume load than compositions of the prior art.

It is a further object of the present invention to provide a method for treating subjects with TBI.

It is an object of the present invention to provide a method of manufacturing oil-in-water emulsions comprising progestogen.

SUMMARY ~~OF THE INVENTION~~

The present disclosure~~invention~~ provides pharmaceutical compositions comprising progestogen, such as progesterone, wherein said compositions are in the form of an emulsion comprising an aqueous phase, an oil, and a surfactant. The disclosed compositions ~~of the present invention~~ advantageously have a low oil content, are ready-to-use, heat-sterilizable, storage-stable, and safe to administer by injection.

The present disclosure~~invention~~ also provides methods for parenteral administration of the disclosed pharmaceutical compositions ~~of the present invention~~. Such methods advantageously expose the subject to which they are administered to a lower lipid level than compositions of the prior art. The compositions ~~of the present invention~~disclosed herein advantageously enable a higher concentration of progestogen to be delivered per unit oil and/or volume, to a subject in need thereof.

The present disclosure~~invention~~ is also directed to methods of treatment of central nervous system conditions, and especially traumatic brain injury, with the disclosed compositions ~~of the present invention~~, and to a method of manufacturing the pharmaceutical compositions ~~of the present invention~~.

In one aspect, the invention provides a sterile, ready-to-use, pharmaceutical oil-in-water emulsion composition for parenteral administration comprising:

- 0.015 to 0.5% wt./vol., preferably 0.05 to 0.4% wt/vol. progesterone;
- 0.5 to 10% wt./vol. of oil, wherein the oil comprises at least 85% wt./wt. triglyceride;
- 0.0425 to 4.1% wt./vol., preferably 0.064 to 3.4% wt./vol. of phospholipid;
- 80-99.4% wt./vol. aqueous medium;

wherein the composition has an osmolality in the range of 200-1000 mOsm/kg, and wherein the emulsion contains no more than 1.2% wt/wt of polyethylene glycol 15-hydroxystearate.

In another aspect, the invention provides a method of manufacturing a composition as defined herein, said method comprising the steps of:

a. combining water, phospholipid and optionally an osmotic agent to produce an aqueous composition;
b. combining progesterone and oil to produce an oily composition;
c. combining the aqueous composition and the oily composition followed by homogenization to form a homogenous oil-in-water emulsion.

DETAILED DESCRIPTION OF THE INVENTION

The present invention provides pharmaceutical compositions comprising progestogen, wherein said compositions are in the form of an emulsion comprising an aqueous phase, an oil phase, and one or more surfactants.