Author's response to reviews

Title: Kinetic stability of all-in-one parenteral nutrition admixtures in the presence of high dose Ca2+ additive under clinical application circumstances

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Author's response to reviews: see over
Dear Editor,

Thank you very much for the referees’ positive comments concerning our paper. We agree with the referees’ remarks and modified the manuscript accordingly. The additional remarks and corrections are highlighted with green color in the revised version of the manuscript.

Please, find below our answers to the referees’ questions and the revised version of the manuscript.

Yours sincerely,

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Response to reviewers

Thank you very much for the valuable remarks and the positive decision.

Answers to the remarks of Reviewer 2

1. There are "special conditions" -please, explain

There are special conditions [e.g. high risk of tetanic contraction or electrolyte depletion in case of cardiac surgery with extracorporeal circulation] when extra electrolytes are needed.

2. ....repulsive and attractive forces.. - Please, specify these forces.

The stability of this system depends on the repulsive and attractive colloidal forces, such as van der Waals, electrical double-layer and steric forces that act between the droplets.

3. ... The three-chamber bags were reconstituted according to the instruction for use...- Unclear, please describe the procedure.

The three-chamber bags were reconstituted according to the instruction for use by breaking the non-permanent seals between the compartments and then mixing them by inverting the bag [10].

4. Test mixtures signed with C contain ca. 50% more Ca\(^{2+}\) than maximally advised by the manufacturers - ....50 % more... why not other %?, Please explain.

Test mixtures signed with C contain ca. 50% more Ca\(^{2+}\) than maximally advised by the manufacturers and it was considered the possible upper limit of Ca\(^{2+}\) content in the comparison of the stability of different mixtures.
5. For zeta-potential measurements we took samples from the middle of the container and sampling was done at start, \textit{after 1, 2, 3, 10, 11, 12 hours} and in the end of the study period (24. hour). \textbf{Why did you choose these time points?}

For zeta-potential measurements we took samples from the middle of the container and sampling was done at start, \textit{after 1, 2, 3, 10, 11, 12 hours} to \textbf{simulate the real parenteral nutrition conditions} and in the end of the study period (24. hour). (Simulation of the nutrition-break-nutrition periods)

6. Until the background is not cleared in case of these mixtures the use of lipid filter in the course of the parenteral nutrition is advised. \textbf{Please, clarify meaning and rearrange the sentence.}

We have rephrased the text.

\textbf{Until the destabilizing component is not identified and the consequent different aggregation behavior of the two types of TPN is not clarified, the lipid filter usage is advised in the course of the parenteral nutrition.}

7. Total parenteral nutrition: TPN - TPN: total parenteral nutrition; \textbf{please list abbreviation first}

We fully agree with the comment and modified it accordingly.

8. In Reference 7 - \textbf{Please, omit the automatic underline.}

We corrected it in the revised version of the paper.

9. In Reference 12 - \textbf{Please, add access date and year.}

We added the access date and year to the reference in the revised paper.

10. \textit{Table 1} - \textbf{Please, format table and add:}

\begin{tabular}{l}
\textit{-in horizontal direction- Droplet size and intensity ratio} \\
\textit{-in vertical direction- Sample}
\end{tabular}

We fully agree with the comment and formatted the Table accordingly.

11. \textit{Table 2} - \textbf{Please, format table and add:}

\begin{tabular}{l}
\textit{-in horizontal direction- Nutrition period (hours)} \\
\textit{-in vertical direction- Mean surface charge (mV)}
\end{tabular}

We fully agree with the comment and formatted the Table accordingly.