Author’s response to reviews

Title: Evaluation of the Safety and Efficacy of a Novel Product for the Removal of Impacted Human Cerumen

Authors:

Joseph Griffin (joe@eosera.com)

Douglass Fullington (dfullington@villagehealthpartners.com)

Jenny Song (jennyhsong@msn.com)

Antoinette Giles (jgiles@villagehealthpartners.com)

C. Anderson (eric.anderson.tx@outlook.com)

Waley Hua (waleyh@gmail.com)

Xiaowen Guo (guoxiaowenok@gmail.com)

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Author’s response to reviews:

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Dr. Jaydip Ray

BMC Ear, Nose and Throat Disorders

Dear Dr. Ray,

Thank you for the opportunity to address the points brought up by the reviewers. Please find attached our point-by-point responses along with the revised manuscript and tables.

We hope you will now find the article suitable for publication in BMC Ear, Nose and Throat Disorders.

Please don’t hesitate to contact me should you require further information.
Kindest regards,

Joseph Griffin, PhD  
Eosera Inc.  
1200 South Freeway Suite 132  
Fort Worth, TX 76104  
Email: joe@eosera.com  
Phone: 516-400-3277

Editor Comments:

Thank you for submitting this article for consideration for publication in BMC Ear Nose and Throat Disorders.  
Unfortunately this is not yet of a standard ready for acceptance for publication.  
Please see the reviewer comments. We look forward to receiving a revised manuscript addressing the reviewer’s comments.

Reviewer reports:

Saeedia Khwaja (Reviewer 1): Nice study. Small number to show anything more than it helps.  
- Author needs to be clear in the statement that this ear product is an adjunct to irrigation.

Thank you for bringing this to our attention. We completely agree, the product was instilled into the ear canal prior to irrigation with warm water. The abstract has been updated along with other areas within the article.

Abstract.

The product is designed to be instilled into the ear canal prior to irrigation with warm water.  
Page 7, paragraph 2
- As this study does not show the ear product dissolving the wax alone. It is compounded by the fact that a placebo or irrigation alone can produce 40 percent improvement as stated in the paper.

We have updated the discussion to reflect some additional data in a second article under peer-review that compared the current product to existing commercially available products.

A previous study compared the new product with two commercially available products, which both contained carbamide peroxide 6.5%, for their efficacy as cerumenolytic agents in vitro [34]. The cerumen samples exposed to the product containing sodium bicarbonate, glycerin, and other buffering agents demonstrated significantly greater disintegration than the carbamide peroxide products at all the time points examined (5, 10, 15, and 30 minutes). Moreover, the cerumenolytic activity of new product was observed within 5 minutes. Although the current study was not comparative in nature, these in vitro results suggest the further controlled comparative clinical studies with the new formulation and other available treatments are warranted. Page 19, paragraph 2

- Hence the outcome is comparable to other products but cannot state better without a comparison trial.

We agree with the reviewer and intended to add more emphasis to this point. A larger, comparative, preferably multicenter trial could address this shortcoming.

However, these shortcomings can be addressed in a larger comparative multicenter randomized masked clinical trial. Page 22, paragraph 1

- I think if the article is rewritten as a safety and efficacy trial then it is acceptable and as stated further studies are needed to compare to other ear products.

We agree, and this was the intention of the study. We have changed the title to focus on safety and efficacy. The abstract purpose now focuses on safety and efficacy.

This open-label study evaluated the safety and efficacy of a novel product for the treatment of impacted cerumen in adult patients. Page 2, paragraph 1
- It should also state that this product was assessed as an adjunct and not as a stand alone product.

We agree and incorrectly assumed this would be understood since all topically applied products are to be rinsed out after. We should have included clarification.

The product was instilled into the ear canal prior to irrigation with warm water. Abstract. The product is designed to be instilled into the ear canal prior to irrigation with warm water. Page 7, paragraph 2

- The graphs are fine. The tables are difficult to follow and maybe better represented in flow chart form.

Upon re-review, we understand the confusion and have attempted to clarify the titles of each table. Given the complexity of the different data points, a flow chart was a challenge.

Table 5 is incorrectly labeled as ‘1st Treatment’, this should read ‘2nd Treatment’. Table 4 will also be clarified to read ‘1st Treatment’. These 2 tables (4 and 5) are the key results and support the contents described in the treatment efficacy section.

Vikas Malik (Reviewer 2): Kindly make following changes:

1. Page 7, line 3 - change use if ear candles to use of ear candles

   Thank you for pointing this out. This was corrected.

2. Page 8, line 57 - How were the depth and the volumes impacted calculated on otoscopic examination especially in cases with severe cerumen impaction with complete or almost complete occlusion of ear canal?

   These were evaluated with an otoscope. We depended on the expertise of the Principal Investigator, a practicing Internal Medicine physician with emphasis in Gerontology, to help us define the grading scale. Since there have been only a few published studies on this topic, we used his expertise along with the published studies to create this scale. Since this was only a single investigator, the grading scale was deemed acceptable. For future, larger, multi-center
studies, our plan would be to gather sufficient reproducibility to allow for publication and validation of this scale.

3. Page 10, line 41 - change self assessment on otological symptoms to self assessment of otological symptoms

Thank you for pointing this out. This was corrected.

4. Page 12, line 58 - Which statistical test was used? Was it Pearson's Chi Square test or the McNemar test?

Both methods were used in the statistical analysis. McNemar test is particularly for outcome variables that have only two responses (i.e. Yes or No, Male or Female). The method was denoted in each table footnote in the statistical report.

The manuscript included only one table that involved a formal hypothesis test as Figure 1 in the manuscript.

P12, line 58 – added clarification as underlined:

For within-subject/ear before-after treatment comparisons, Pearson’s Chi-square test, or McNemar test for dichotomized variables, was used.

P17, Line 4- 6- added clarification as underlined:

…observed after treatment for decreased hearing (P = 0.209 per McNemar test)…

5. Page 14, line 54 - you mention two patients reported dizziness. Did this resolve following removal of cerumen? If not, then was it related to cerumen impaction?

For this study, dizziness was defined as a non-otological symptoms associated with earwax impaction. During this study the subject’s perception of dizziness, restlessness, anxiety, and impact on their overall quality of life were solicited from the subjects before and after treatment. All the responses were recorded as a Yes, No, No Opinion or NA response. These 2 patients reported this before the initiation of treatment and did not report after treatment.
6. Page 19, line 33 - change allowed upto 2 15 minutes treatments to allowed upto two 15 minutes treatments

Thank you for pointing this out. This was corrected.