

Response letter

Dear Ze-Mao Gong,

We revised and updated the manuscript according to comments and suggestions for **Manuscript Revision-Observational Study**.

The manuscript was written and supervised by Prof Loening-Baucke, who is native American and emeritus of Iowa University (Gastroenterology).

The biostatistics was performed by coauthor Christopher Gille, who is responsible for biostatistics in Department of Biochemistry, Charite.

There is no conflict of interest or data to share.

We hope you will find the revised manuscript appropriate for the publication in World Journal of Gastroenterology.

Best wishes

Alexander Swidsinski

Point by point response to specific reviewer comments:

Dear Sir, I read your manuscript with great interest and I think the information you found is of great value. However, there are some questions that you should clarify:

a) Can you describe the content and quality of the humic acids contained in "activomin"?

Activomin ist the only medical product based on humin acids which is trademarked in a Germany since 2006 and is freely available in stores. One capsule contains 400 mg of humic acids. We have no technical documentation on it composition or know details on its production.

There are two journal research that suggest the safety of the presence of humic acids in the water (Oliver, Barry G. "Dihaloacetonitriles in drinking water: Algae and fulvic

acid as precursors". Environmental Science & Technology. 1983;2: 80. Peters, Ruud J.B.; De Leer, Ed W.B.; De Galan, Leo. "Dihaloacetonitriles in Dutch drinking waters". Water Research. 1990;24: 797).

b) What kind of research have you done regarding the safety of the product?

The safety of the certified products is regulated by TUV in Germany and was not purpose of our study. The manufacturer sent us the copy of the certificate which is attached.

c) How long has a person taken "activomin" with a proper follow up?

What is the maximum dose taken per day? How has that dose been calculated? I could not find this information anywhere. Hope you can let us know the answers to these questions, as soon as possible, in order to publish it.

In our study 3 x 800 mg Activomin® were taken orally for 10 days followed by 3 x 400mg for 35 days. We were not interested in a dose finding study, but wanted to see, whether any effects on colon microbiome can be observed. For these reasons we used the dosis recommended by manufacturer. No follow up controls were performed.