Review Form 1.6

Journal Name:	**European Journal of Nutrition & Food Safety**
Manuscript Number:	**Ms_EJNFS_69613**
Title of the Manuscript:	**FERMOTEIN DOES NOT EXERT GENOTOXIC EFFECTS IN BACTERIAL REVERSE MUTATION AND IN VITRO MAMMALIAN CELL MICRONUCLEUS TESTS**
Type of the Article	**Original Research Article**

General guideline for Peer Review process:

This journal's peer review policy states that **NO** manuscript should be rejected only on the basis of '**lack of Novelty'**, provided the manuscript is scientifically robust and technically sound.
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PART 1: Review Comments

	Reviewer's comment	**Author's comment** *(if agreed with reviewer, correct the manuscript and highlight that part in the manuscript. It is mandatory that authors should write his/her feedback here)*
Compulsory REVISION comments	1. Add line numbering in the manuscript to facilitate any revisions and / or corrections; 2. Repetitions in the introduction (1st and 2nd paragraph) carefully double check the text; 3. Introduction too short and not very thorough: expand introduction with more bibliographical references and more information about the study in question; 4. How many slides were read for the NM test? 5. How many cells (BN) in total were counted for each slide? 6. How was the CBI calculated? 7. Why did the authors not follow and cites the *Fenech* protocols other than OECD guidelines (Fenech, M. (2007). Cytokinesis-block micronucleus cytome assay. Nature protocols, 2 (5), 1084)? 8. We speak of genotoxic damage referring to the formation of MN and cytostasis / cytotoxicity referring to the CBI, why were NBUD's not also observed as an index of genotoxic damage? NBUD's are generally considered in this type of test, as they are also biomarkers of genotoxicity. there are another nuclear anomalies such as nucleoplasmic bridge and NBUD's. Every marker evolved into the CBMN cytome assay. Amplified DNA is localized to specific sites at the periphery of the nucleus and is eliminated via NBUDs during S phase of cell cycle. NBUDs have the same morphology of MN but they are connected to the nucleus by narrow of nucleoplasmic material. 9. Is it possible to provide an image of the cells observed under the microscope during CBMN assay? (BN cell with MN)	1. We added line numbering to the document. 2. The first paragraph should not have been included in the manuscript. We agree with the reviewer that, when including this paragraph, there is repetition of information. Therefore, we removed the first paragraph from the manuscript. 3. The introduction was expanded with several bibliographical references and more information about the study is now provided as the last paragraph of the introduction. 4. As stated in the manuscript on page 4, line 106, experiments were performed in duplicate. For each condition or dose tested, two slides were used (see page 4, line 120-121). This has also been described in table 5 (n = 2) and the same information has been added to table 4. 5. The total number of cells counted is described in the title of table 5: "Total number (n = 2) of mononuclear (MN) or binuclear (BN) cells with micronuclei per 2000 cells". To clarify, the number of cells counted per duplicate was included in the same table description. Footnote C of Table 5 also describes that the 'total number of cells with micronuclei is the sum of two duplicates (counts per duplicate indicated between brackets)'. 6. The CBPI was calculated according to Annex II of the OECD guideline. At page 4, line 124, this reference has been added to clarify. 7. OECD guidelines were leading since OECD-compliant studies are requested for regulatory approval procedures. This has been clarified on page 3, line 70. 8. According to the OECD guideline, measurement of nuclear buds is not by standard included in the assessment of genotoxicity by the micronucleus test. Since experiments were performed according to OECD guidelines, measurement of nuclear buds were not included. 9. We do not have an image of the cells observed under the microscope. In addition, we feel that an image does not contribute to the manuscript and we therefore prefer to not include one.
Minor REVISION comments		
Optional/General comments	The manuscript is very well written, so I encountered some minor rather than methodical editorial errors. The manuscript is adequately divided, the abstract is concise, I found several repetitions in the introduction, moreover the latter is quite poor in information and bibliographical references. The need for this study must be well addressed in the Introduction section in detail. The important experimental conditions and the number of samples for each data must be clearly provided. The manuscript should be implemented in the introduction and checked more carefully. The author is also encouraged to add recent research findings to best justify this study. After all corrections, the manuscript can be accepted for publication.	The first paragraph has been removed from the introduction, resulting in less repetition. The introduction was expanded with several bibliographical references and the objective and need of the study is now described at the new last paragraph of the introduction. The requested experimental conditions and the number of samples for each data are provided.

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PART 2:

	Reviewer's comment	**Author's comment** *(if agreed with reviewer, correct the manuscript and highlight that part in the manuscript. It is mandatory that authors should write his/her feedback here)*
Are there ethical issues in this manuscript?	*(If yes, Kindly please write down the ethical issues here in details)*	