Review of: "A Review of the Scientific Literature on Experimental Toxicity Studies of COVID-19 Vaccines, with Special Attention to Publications in Specific Toxicology Journals"

Harpreet Singh[1,2]

1 Division of Development Research, Indian Council of Medical Research, New Delhi, India
2 Faculty of Medical Sciences, Academy of Scientific and Innovative Research, New Delhi, India

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General Comments

1. The review comprehensively analyzes nonclinical studies on the adverse effects of COVID-19 vaccines, highlighting the scarcity of published data from major mRNA vaccine manufacturers. This gap raises questions about transparency and the publication practices of these companies, which could hinder informed decision-making and trust within the scientific and medical communities.
2. The lack of clear categorization based on vaccine technology (e.g., mRNA, viral vector, protein subunit) limits practical insights. For instance, combining data from these different vaccine types without distinction makes it difficult to assess whether certain adverse effects are specific to a particular technology. This lack of clarity impedes targeted follow-up studies and regulatory recommendations that could be more effectively tailored to each vaccine type's unique mechanisms and potential risks.
3. The absence of specific quality and relevance criteria for the inclusion of studies reduces the overall rigor. Without these criteria, there is a risk of including low-quality studies that could skew findings or lead to biased conclusions. This makes it challenging to establish a consistent benchmark for nonclinical safety data across the studies reviewed.

Specific Comments

1. Clarify the distinction between clinical and nonclinical studies and why data from nonclinical studies in animal models are crucial for predicting vaccine safety in humans. This would provide better context for readers about why this review focuses on animal-based research.
2. To improve the rigor of the review, consider applying specific criteria for evaluating the quality and relevance of the included studies. For example, use standardized checklists like the *SYRCLE's risk of bias tool* for animal studies or ensure that all studies included have a clear description of experimental design, sample size justification, and statistical analysis.
3. Since mRNA vaccines (e.g., Pfizer/BioNTech and Moderna) were among the first COVID-19 vaccines deployed globally and have generated significant public interest, separating their data from other vaccine technologies would allow for a more targeted analysis. This could reveal specific safety trends, such as differences in immunogenicity or

adverse effects unique to mRNA platforms versus viral vector or protein subunit vaccines.

4. Enhance Table 1 by including an additional column that specifies the type of vaccine technology (e.g., mRNA, viral vector, protein subunit). This would help readers quickly identify trends and differentiate between the safety profiles of different vaccine technologies, improving the table's utility as a reference.
5. Expand the discussion on how species-specific responses can vary, particularly when comparing results from rodent models to those from non-human primates. For example, the immune and metabolic differences between species can lead to variations in the manifestation of adverse effects, limiting the direct applicability of these findings to human safety assessments.