

ANSWERS TO REVIEWERS' COMMENTS AND CHANGES IN THE REVISED MANUSCRIPT

Reviewer 1 - Reviewer's code: 03505676

Comment 1

The association between chronic liver diseases and HCC in the VCM workers should be discussed because some chronic liver diseases are also the risk factors for HCC.

Answer

In the revised manuscript, it is specified that the presence of liver cirrhosis increases the risk of HCC independently from its etiology through multiple mechanism, including chromosomal instability (page 4).

Comment 2

Possible mechanisms on the relationship between VCM and HCC or chronic liver diseases should be mentioned.

Answer

In the revised version of the paper it has been added that vinyl chloride is mutagenic, causing an increased frequency of chromosomal aberrations, micronucleus formation, sister chromatid exchange, Ki-ras and p53 gene mutations (page 4).

Reviewer 2 - Reviewer's code: 02936110

Comment 1

The title of this paper is Occupational exposure to vinyl chloride and liver diseases, however, only vinyl chloride, hepatocellular carcinoma and Chronic liver disease are discussed in this review. Whether there are any new epidemiological studies about vinyl chloride and angiosarcoma, if there are, please supply it.

Answer

Results of recent papers did not add much knowledge about the already well-established association between VCM and angiosarcoma. Recent papers distinguishing between angiosarcoma and HCC mainly demonstrated a longer latency for HCC; this issue was summarized in the previous version and some detail has been added to the revised manuscript (page 5).

Comment 2

What's the morbidity of hepatocellular carcinoma, angiosarcoma and chronic liver disease in the workers exposed to vinyl chloride.

Answer

There are sparse data to estimate the overall impact of morbidity from all liver diseases among vinyl chloride workers. However, according to our last publication (Am J Ind Med 2019;62:14-20), among workers in the highest exposure category as much as 29% (16/56) of overall deaths were due to liver cancer (all types) or liver cirrhosis. This has been added to the revised manuscript (page 7, beginning of the Conclusion section).