Joint Statement on Hepatitis C Human Challenge Studies

Draft copy. Final copy published in The Lancet Gastroenterology & Hepatology, *September 2023.*

We, the 121 undersigned, believe that human challenge studies among adult volunteers will be critical in the development of hepatitis C vaccines. Among us are experts in hepatitis C, vaccinology, immunology, philosophy, bioethics, and public health, advocates for people who inject drugs and other at-risk groups, and advocates for challenge study volunteers.

Despite the advent of safe and highly effective direct-acting antiviral (DAA) treatments, the ongoing toll of hepatitis C remains high among low- and middle-income countries and vulnerable populations such as people who inject drugs. Millions of new infections occur annually, outpacing cures in some regions,[1] with progress further disrupted by the COVID-19 pandemic. Without a change in strategy and the development of new tools, we will not reach the ambitious goal set out by the World Health Organization of elimination of viral hepatitis as a public health threat by 2030. This will require an effective hepatitis C vaccine — "the best insurance for the future," as highlighted by a recent announcement of the White House National Hepatitis C Elimination Program.[2]

Development of a hepatitis C vaccine with the objective of preventing chronic hepatitis C virus infection and its long-term health consequences will be challenging. While the diversity of the virus is a problem that will require innovative vaccine designs, the remarkable strides in vaccinology that were seen during the COVID-19 pandemic hold promise that the scientific challenges can be overcome. Perhaps more difficult than making a vaccine is proving that it works. Testing vaccines in the traditional model for hepatitis C is impractical. Ethical considerations, funding moratoria, and legal barriers now prevent testing in chimpanzees, the only other creature naturally susceptible to the virus. In the absence of satisfactory alternative animal models, researchers are left with large-scale trials in humans.

The most recent trial, a formidable effort to test the ChAd3-NSmut and MVA-NSmut vaccines in people who inject drugs, demonstrated the serious limitations of this strategy. The phase 1/2 trial took nearly six years and tremendous effort to complete. The vaccines unfortunately proved ineffective.[3] Not only was this disappointing for the field, but it may also have engendered significant reluctance among vaccine developers to pursue hepatitis C vaccines given the formidable challenges to study even the most promising candidates.

During those six years, millions contracted hepatitis C worldwide, many of whom will eventually die as a result. In 2017 alone, the disease killed an estimated 580,000 people — an average of over 1,500 every day.[4] With mortality so high, time is of the essence.

Human challenge studies for a hepatitis C vaccine could accelerate vaccine development dramatically. The effort to establish the model and test an initial vaccine candidate could take as little as three years. If that candidate fails, subsequent studies to test others could provide evidence of efficacy as quickly as one year.

It is only because of the remarkably effective treatments that we can now consider human challenge studies for hepatitis C. With DAAs, cure rates of people without cirrhosis are reliably over 98%, with highly effective salvage regimens for the few who do not respond to a first course of therapy.[5, 6] We are confident that in the era of DAAs, human challenge studies can be done in accordance with the highest ethical and safety standards. Healthy volunteers providing fully informed consent would be infected for at most six months before treatment and would be free to go about their lives with the right to request treatment and withdrawal from a study at any time. Acute infection causes no or few symptoms in most, and unlike in most challenge studies, where the risk of transmission necessitates quarantine of participants, the risk of passing hepatitis C to others is very low in day-to-day life.

The impact of a vaccine would be enormous: reducing transmission, preventing cirrhosis and most importantly, markedly reducing the rate of liver cancer, the world's second-most deadly cancer in terms of total fatalities.[7] The global success of hepatitis B vaccine in achieving these goals exemplifies the importance of an effective hepatitis C vaccine. With the prospect of such a significant advance, we have confidence that people will volunteer to participate in hepatitis C challenge studies, and with such a strong team of experts worldwide, we are confident this approach will lead to the development of a successful hepatitis C vaccine.

We are excited about the prospect of human challenge studies to advance vaccine development and are eager to work carefully and deliberately with funders, regulators, and all other stakeholders to bring them to fruition.

Signed:
HCV CHIM Open Letter Signatories
Institutions are listed solely for identification purposes and do not represent their endorsement of this letter.

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