U.S. FOOD & DRUG ADMINISTRATION

April 25, 2023

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Dear Mr. Siri, Ms. Brehm, and Mr. Stavola,

This is in response to your March 6, 2023, letter to FDA, CDC, and NIH. We have reviewed the information and claims from your letter and the literature, and have concluded that COVID-19 vaccines cannot be the predominant reason for increased mortality during the pandemic as suggested. Our reasons are as follows:

1. You use modeling of excess mortality data to claim an increasing death rate, but a careful review of the models and the current data indicate the opposite.
2. Several peer-reviewed studies from the FDA and others show that there is no link between vaccination and a higher death rate in general.

Our detailed review of the information in your letter can be found below.

The Informed Consent Action Network (ICAN) expressed concern over the potential increasing trend of mortality rates among young and middle-aged people globally in the past one to two years. In your letter by the authors Siri, Brehm, and Stavola (hereafter referred to as the authors), ICAN urges the FDA, NIH, and CDC to investigate this issue and publish findings. According to the letter, there has been a statistically significant increase in all-cause mortality, with the highest number of deaths occurring among young and middle-aged individuals. The authors suggest that the spatial and temporal patterns of the increased deaths make it unlikely that COVID-19 is the primary cause. ICAN proposes that the COVID-19 vaccination program may be a contributing factor to this phenomenon.

We appreciate the authors sharing their concerns. This is a critical public health matter, and we take these concerns very seriously. We will address the points made by the authors and provide details regarding the investigations conducted by the FDA in our response below.

1: In *"all-cause mortality – a bias-free indicator which can detect important trends in population level deaths"*, the authors suggest that all-cause mortality is an objective and effective indicator for detecting significant population-level mortality events. We agree with the authors that by analyzing all-cause mortality data, trends and patterns in mortality can be identified, and we can evaluate the impact of various interventions, such as public health campaigns or medical treatments, on mortality rates. However, all-cause mortality data should be carefully analyzed and interpreted so as not to draw erroneous conclusions regarding causes of mortality.

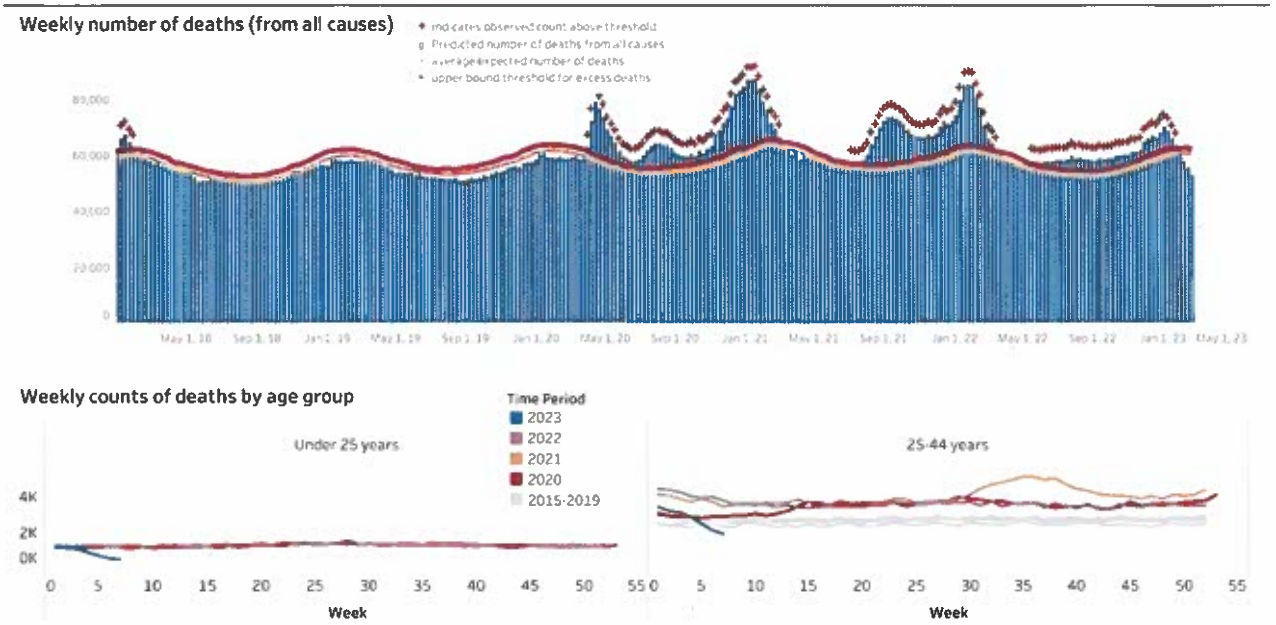

Figure 1: *(Top Row) Weekly excess deaths in the overall population 2018-2023. We would also like to draw the attention of the reader to Summer 2021 and Spring 2022 when COVID-19 circulation in the US population diminished. (Bottom Row) Weekly all-cause counts of deaths by age groups 0-25 years and 25-44 years, plotted by year and compared against baseline pre- pandemic period 2015-2019. It is important to notice the relative stability of weekly counts of deaths in the age group 0-25 years during 2015-2022. Source: Excess Deaths Associated with COVID-19 (cdc.gov).*

2: In *"a significant rise in all-cause mortality is occurring in those young to middle-aged"*, the authors use results from the following sources:

- all-cause mortality modeling data from the European Mortality Monitoring Project (EuroMOMO),
- a manuscript by Rancourt, *et al.*, which has not yet been peer-reviewed,
- a peer-reviewed manuscript by Ludden, *et al.*, published in *Health Care Manag Sci.*,
- a manuscript by Faust, *et al.*, which has not yet been peer-reviewed.

EuroMOMO is a modeling effort where the mortality baseline is estimated using statistical modeling and their model is fitted to a valid historical period as defined by the user. The authors use EuroMOMO cumulative all-cause mortality charts to support their claim of an increasing trend in the young to middle-aged population. However, the authors fail to mention the following important caution provided by the developers of EuroMOMO: "Please note that the cumulated excess mortality outputs for the COVID-19 pandemic period may be unreliable, due to some model issues." Furthermore, EuroMOMO states that "the EuroMOMO mortality surveillance system does actually not detect more deaths among the 0 to 14-years old during the ongoing COVID-19 pandemic than in the period before the COVID-19 pandemic, even if the cumulated outputs reported on the EuroMOMO website suggest so."

Rancourt, *et al.*, uses CDC's US monthly/weekly all-cause mortality data for the period starting in 2000 and ending on February 5, 2022. The underlying data do seem to indicate an increase in all-cause mortality throughout the pandemic until February 2022. However, in March 2023 when we analyzed the same source presented in Rancourt, *et al.*, we see that the trend in all-cause mortality has decelerated and even returned to below pre-pandemic numbers, as shown in Figure 1 above.

Ludden, *et al.*, using provisional mortality reports from the CDC, compute mortality risks for 22 age and sex subgroups in 2021 and compare against 2015-2019 using odds ratios. They report that most age and sex subgroups faced greater COVID-19 and non-COVID-19 mortality risks in April 2020-March 2022 than in 2015-2019 period. This finding agrees with our knowledge and with Figure 1. Similarly, **Faust, *et al.***, estimate excess mortality during the pandemic using data from the CDC for the 2014-February 2022 period, and they present similar results. The authors seem to attribute the increase in non-COVID-19 mortality to non-COVID-19 causes. We would like to note that these two articles cannot definitively establish the cause of the excess deaths. As rightfully pointed out by the authors of Ludden, *et al.*, "though non-COVID-19 excess deaths did not have COVID-19 on their death certificates, the pandemic's societal, economic, and health care system changes likely contributed to many such deaths. Elective surgery postponements, hospital staffing shortages, delayed stroke responses, and other disruptions may have deprived non-COVID-19 patients of life-saving care."

3: In *"possible causes – alarming increase cannot exclusively be due to COVID-19"*, the authors summarize their claims and, to support them, present excess mortality data from Australia, the US, the EU and Canada. The authors write that, "The hypothesis that COVID-19 vaccines may contribute to the rise in excess deaths is not outlandish; Pfizer's own clinical trial data indicated a 24% higher rate of mortality in the vaccinated group versus the unvaccinated." Unfortunately, they fail to mention that none of the deaths in the study were attributed to vaccination.

It is important to analyze disease-specific causes of excess mortality, particularly in younger demographics. For this, the authors present the results of exploratory (linear regression) analyses on global mortality and vaccine uptake rate data. The results of those studies show a correlation between vaccination and excess mortality. This is perhaps expected, as COVID-19 infection, long COVID, lockdown stringencies, healthcare quality, changing healthcare seeking behaviors, excess mortality, COVID-19 vaccination, and many other factors are all somehow interrelated. However, correlation does not imply causation. To understand the extent of the relationship and causality between the COVID-19 vaccination and all-cause mortality, other factors, such as those mentioned in this paragraph, might also be affecting that relationship and should be considered. For example, to study a potential increase in young male mortality during the COVID-19 pandemic, we would need to use the vaccine coverage and mortality data for that age group and normalize the data by the sizes of the vaccinated and unvaccinated populations. Other factors are also at play; for example, because of the protection offered by vaccination, vaccinated individuals may become more complacent and less careful of physical distance and hygiene precautions, whereas unvaccinated people would not. Due to the complex interplay of multiple factors impacting all-cause mortality, in practice, sophisticated statistical methods are used to avoid biased epidemiological conclusions.

A recent FDA study aimed to provide information and context about reports of death to the US Vaccine Adverse Event Reporting System (VAERS) following COVID-19 vaccination (Day, *et al.*, "Reporting Rates for VAERS Death Reports Following COVID-19 Vaccination, December 14, 2020-November 17, 2021." Pharmacoepidemiology and Drug Safety (2023)). The FDA scientists found that the rate of deaths reported to VAERS between December 2020-November 2021 were much lower than the background rates of deaths from all causes in the general population (Table 1). These findings do not suggest a link between vaccination and overall increased mortality. In contrast, a mathematical modeling study estimated that vaccinations prevented 14.4-19.8 million deaths from COVID-19 in 185 countries and territories between December 2020, and December 2021 (Watson, *et al.*, "Global impact of the first year of COVID-19 vaccination: a mathematical modelling study." The Lancet Infectious Diseases 22.9 (2022): 1293-1302). Moreover, Xu, *et al.* ("A safety study evaluating non-COVID-19 mortality risk following COVID-19 vaccination." Vaccine 41.3 (2023): 844-854) demonstrated there are significantly fewer non-COVID-19 and all-cause mortalities following COVID-19 vaccinations in the US in the period December 2020-August 2021 by studying 6,974,817 unique individuals with at least two months of follow-up. This was one of the largest vaccine safety studies of its kind. Across vaccine types and doses and age groups, the non-COVID-19 mortality rates in vaccine recipients were lower than those in the corresponding comparator group.

***Table 1**: Expected rates of death per million vaccinated persons and US death events reported to VAERS per million vaccinated persons within 7 days and within 42 days of vaccination among COVID-19 vaccine recipients, by sex and age—Reports received between December 14, 2020–November 17, 2021.*

	Expected all-cause deaths		Observed reporting rates for US death events							
			All COVID-19 vaccines		BNT162b2 vaccine		mRNA-1273 vaccine		Ad26.COV2S vaccine	
	7-day	42-day	7-day	42-day	7-day	42-day	7-day	42-day	7-day	42-day
Sex										
Female	159.3	956.0	14.5	23.4	10.9	17.8	19.2	29.9	19.4	37.4
Male	172.0	1031.7	20.5	32.7	15.3	24.1	27.4	44.0	22.2	37.5
Age (years)										
5–14	2.6	15.6	0.3	0.8	0.3	0.8	0.0	0.0	0.0	0.0
15–24	14.2	85.1	1.8	2.8	1.6	2.4	1.9	3.1	4.4	6.3
25–34	25.5	152.7	2.8	4.0	2.2	3.2	3.4	5.0	4.1	6.1
35–44	37.4	224.5	4.6	7.3	3.5	5.6	5.8	8.5	6.2	13.5
45–54	77.0	461.7	8.1	12.4	5.5	8.9	10.1	14.6	13.3	21.7
55–64	169.8	1018.6	16.0	24.6	12.5	19.5	18.5	26.4	24.3	44.5
65–74	343.2	2059.4	27.8	44.7	23.9	38.8	29.8	46.4	42.1	80.5
75–84	857.2	5143.0	51.1	86.3	43.6	74.2	54.6	90.8	91.6	179.3
≥85	2601.4	15608.3	178.0	292.3	170.8	268.6	179.6	309.3	212.1	363.5
Total	165.6	993.3	17.3	27.8	13.0	20.8	22.9	36.3	20.7	37.1

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The FDA and the CDC are monitoring the safety of authorized and licensed COVID-19 vaccines through both passive and active safety surveillance systems. Based on available information, FDA strongly finds that the known and potential benefits of the COVID-19 vaccination greatly outweigh their known and potential risks. We reviewed the author's concerns regarding mortality rates among the young and middle-aged groups; however, the claim of a predominance of vaccine-associated excess mortality during the COVID-19 public health emergency is unsubstantiated.

Sincerely,

Lorrie H. Mcneill -S Digitally signed by Lorrie H. Mcneill -S Date: 2023.04.25 19:04:09 -04'00'

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