Questions for the Panel on Regulatory Processes

- **EMA now makes recommendations on the use of COVID vaccines beyond the indications. Do your think it could be a conflict of interest knowing that the primary responsibility of the EMA is a regulatory agency and it is not in charge of public health policy?**

  Hector S Izurieta: I would not really call that a "conflict of interest" but differences in institutional roles. To use the example of FDA and CDC: we are both public health institutions, and thus our interests are the same, none of our institutions have any commercial or personal interests at stake and we serve the same community. In the U.S., the regulator provides the license and the indication, and CDC makes recommendations for use. Although these decisions are in principle independent, we do talk to each other and consult very frequently, always trying to harmonize as much as possible.

- **How many new vaccines have you rejected during the authorization process? Or all vaccines presented for authorization met the standards of quality, safety and immunogenicity? What proportion of vaccines of vaccines got approval and what proportion did not so far?**

  Hector S. Izurieta: A number of vaccines have of course been rejected during the authorization process by the FDA, that decision is called a "complete response" (CR). That said, a license application (BLA) rejected means that a huge amount of review time has been spent by the FDA that could have been used in other products to help the US population in the prevention of disease. It also means of course a huge time and effort lost by the Sponsor. So, the ideal scenario is for the Sponsor not to submit a file that is not ready or appropriate. FDA has processes in place to help with this, including bu not limited to type C meetings. However, any Sponsor is free to make a BLA submission, and the contents of the submission are their responsibility.

- **Any thaughts on strategy campaigns to try to educate the populace (and discredit misinformation) so regulatory decisions can be trusted by the majority?**

  Hector S. Izurieta: Providing the most accurate information in the most transparent way as soon as we have it is our best strategy. That said, misinformation campagns (usually driven by specific interests) are dificult to fight. Improving the level of education for everybody, and their capacity for critical thinking is essential, that should ideally start early in life.

- **Do we still need EUL vaccines since there is no more (COVID) pandemic? Do we allow more time for subsequent vaccines?**

  Hector S. Izurieta: For this reason, we are not issuing EUAs for any new vaccines. However, for vaccines that were already under EUA, we have continued to use the EUA approach for age/risk groups for which we don't yet have the information necessary for issuing a supplementary Biologics License Application (sBLA).

- **How are regulators approaching the need for primary vaccination in children for COVID 19 in the setting varying degrees of seroprevalence and hybrid immunity across different age groups and countries? How would you handle this issue?**

Hector S. Izurieta:

In general, it would be "safer" for FDA to wait until a biologics license aplication (BLA)is accepted to make any decision. However, the lack of a decision, or its delay, is by itself a decision and has consequences, this is particularly relevant in the setting of a pandemic.

So, we have issued EUAs for vaccination of children of different age groups as soon as we have obtained and evaluated the information on benefits and risks we needed for each group. For that purpose (EUA), we have shortened the duration of safety follow-up from six months (required in a BLA) to a- least two months. Also, an EUA can be withdrawn when additional information made available guides us towards that decision. For some age groups, some information from one age (e.g. immunogenicity, safety) can be extrapolated to another under certain conditions.

Regarding hibrid immunity: We are taking the information on hybrid immunity into account (the immunity provided by vaccination + prior infection). The studies to which I have contributed do suggest that hybrid immunity is more effective than infection alone or vaccination alone. Other studies suggest the same.

Of course, for a person to have hibrid immunity, he/she must have survived the initial natural infection, and that would be dangerous without the help of a prior vaccination. What I mean is that I would not recommend to a person who has never been exposed to the wild virus to get exposed to it instead of getting first exposed to the much safer vaccine virus.

That said, as of now, a large majority of the US population that has survived the pandemic so far has already had both prior vaccination + a prior infection, so they already have hybrid immunity. That information is being considered for regulatory decision-making.