WEEKLY EPIDEMIOLOGICAL REPORT

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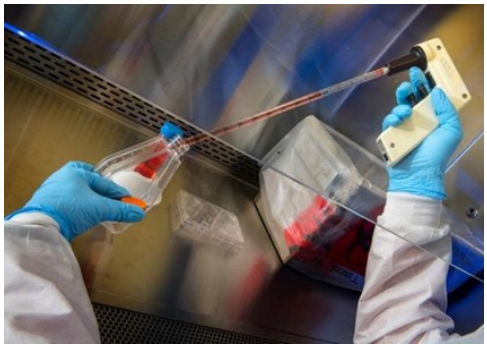
Ethical considerations in clinical trials of vaccines in public health emergencies



Source: CDC

Vaccines have become one of the most powerful tools in the 20th century against many diseases. When novel pathogens like coronavirus (COVID-19) emerge, the global community is under threat of control due to the increased international movements among the global population in the current context. Hence known and unknown pathogens continue to distribute rapidly and develop disease epidemics and pandemics that challenge the human population.

Vaccines were developed as one of the major preventive methods to control pandemics such as in the recent COVID-19 situation. When conducting vaccine trials during public health emergencies, unique ethical challenges arise due to the urgent need for a product. Yet a vaccine cannot be developed rapidly. It typically involves many years of scientific research leading to extensive clinical trials. Generally, the research collaborators from high-income countries combined with the participants in different settings. The different stakeholders involved are mostly multinational. Different countries involved may have unique ethico-legal frameworks, fragile health systems, and diverse cultural contexts with variable capacities. Further, the studies can be done with complex designs and invasive procedures. The combination of these factors gives rise to ethical dilemmas in conducting vaccine trials.

Generally, "Human challenge trials" are conducted in pandemic situations. Because "Human Challenge Trials" are easier and quicker in identifying results. Yet, ethical dilemmas may outweigh efficiency. The suitability of a novel health product during public health emergencies is assessed by "The emergency use listing (EUL) procedure".

The WHO EUL is a risk-based procedure for "assessing and listing unlicensed vaccines, therapeutics and in vitro diagnostics". It will assist the interested UN procurement agencies and member states in determining the acceptability of the products.

The objective is to make available the medicines, vaccines or diagnostics as rapidly as possible to the public to control the epidemic/ pandemic while ensuring the adherence to stringent criteria of safety, efficacy, and quality of the product.

The EUL pathway involves a thorough assessment of late phase II and phase III clinical trial data with additional data on safety, efficacy, and quality with a risk management plan. Independent experts and WHO teams review these data and consider the current body of evidence on the vaccine is under consideration.

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The company producing the vaccine must commit to continuing to provide data to enable full licensure and "WHO prequalification" of the vaccine as part of the EUL process. This "WHO prequalification process" will assess the additional clinical data produced from vaccine trials to ensure the vaccine meets the necessary standards of quality, safety, and efficacy for the population.

With the evolvement of new vaccine development in the recent past scientific and ethical requirements in vaccine trials faced difficulties in implementation. According to the comprehensive 2017 report of the "National Academy of Sciences" confirmed, the substantive ethical requirements governing research with humans do not change even in emergency circumstances.

The benefits of science to improving human health should always be considered within the context of ethical principles. We should make use of the evidence provided by the recent epidemics to expand our understanding of this field and new aspects that we recognize to be necessary to the ethical assessment of vaccines. The ethical principles of autonomy, beneficence, justice, and non-maleficence should be adhered to. There are many ethical challenges arising classified into safe and standard manufacturing and obtaining ethical approval, evaluation and monitoring of safety and efficacy, mass production & fair distribution, and public acceptance.

Autonomy

Autonomy is respecting freedom of thought and action; In vaccine trials should always respect autonomy and take special steps to protect the vulnerable. The ongoing outbreaks may urge researchers to speed up, shorten, or modify informed consent procedures. For example, the presence of severe risks to populations during an epidemic may limit the ability of human subjects to give legitimate consent. However, informed consent is crucial in all instances of clinical trials. Before the consent the provision of information is necessary. It should include various ethical aspects such as side effects, consequences, how to compensate for the damages, use of the placebos, and the participant's ability to make the decision. In the recent COVID-19 vaccine autonomy was challenged in the prioritization of protection against the manipulation of individuals and countries.

Justice

Justice applies to how equitably the vaccines are beneficial to the population. Also, how the clinical trial investigators are enrolling subjects. If they are enrolling disproportionately fewer minorities, it could be argued the trials are not meeting the standard of justice. Justice also applies to how quickly investigational products are made available to the public.

Assuring access to vaccines for all countries at affordable prices is an ethical concern. Producing affordable vaccines, considering countries with limited financial capacity, in order to provide equitable access should be considered in the development process. Misuse of the weaknesses of research ethics in developing countries should be avoided. Non-discrimination and non-stigmatization are an important aspect to be considered in vaccine allocation.

Beneficence

The benefits of the vaccines should be clarified prior to engaging the participants in the trials. Prioritization should be given to the groups who are at high risk of severe disease and mortality. After obtaining the emergency vaccine use approval, the participants should be given the priority of access to the vaccines. It is important to consider vaccines as an essential universal good. The allocations should be based on the logical parameters that are tailored to current needs, which benefit the most.

Non-Maleficence

Harm prevention is an essential part of vaccine trials. Hence adherence to the harm prevention principle is an ethical obligation for vaccination. Need to comply with the ethical requirements for issuing patents to manufacturers and issuing mandatory licenses in emergencies to limit the negative effects on the participants. Patent holders should be monitored regularly and need to obtain strong evidence on the safety and efficacy of vaccines.

In conclusion, ethical complexities need to be considered even in the context of public health emergencies in any vaccine trial.

Compiled by

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Table 1: Selected notifiable diseases reported by Medical Officers of Health 30th– 06th Sep 2023 (40th Week)

RDHS	Dengue Fever		Dysentery		Encephalit		Enteric Fever		Food Poi-		Leptospirosis		Typhus		Viral		Human		Chickenpox		Meningitis		Leishmania-		WRCD	
	A	B	A	B	A	B	A	B	A	B	A	B	A	B	A	B	A	B	A	B	A	B	A	B	T*	C**
Colombo	111	11766	1	15	1	13	0	2	0	12	12	281	0	0	0	5	0	0	14	282	1	39	0	6	**41**	**100**
Gampaha	108	11834	2	21	0	16	0	7	1	6	7	493	0	10	1	17	0	0	9	247	2	108	0	43	**10**	**100**
Kalutara	44	4193	1	23	1	4	0	1	2	18	20	743	0	2	0	10	0	1	15	443	1	88	0	2	**66**	**200**
Kandy	124	6368	1	34	0	2	0	10	2	19	8	255	4	57	0	3	0	2	9	251	0	24	0	26	**90**	**100**
Matale	25	1395	0	4	0	3	0	1	0	29	2	129	0	14	1	7	0	0	1	55	0	7	6	271	**28**	**100**
NuwaraEliya	6	244	1	137	0	4	0	3	0	49	17	143	1	65	0	5	0	0	7	164	4	27	0	3	**62**	**100**
Galle	53	2437	2	45	0	13	1	6	3	32	14	794	1	72	0	2	0	1	14	305	1	26	0	3	**39**	**100**
Hambantota	17	1287	0	11	0	3	0	1	0	9	9	264	0	68	0	9	0	0	3	132	1	19	18	545	**33**	**100**
Matara	20	1657	1	25	0	8	0	1	0	19	4	457	0	32	0	5	0	2	3	267	1	21	4	164	**59**	**100**
Jaffna	50	2084	6	91	0	2	0	12	1	32	0	12	6	512	0	5	0	2	6	163	3	18	0	2	**69**	**93**
Kilinochchi	0	89	3	12	0	0	0	1	0	16	0	8	0	7	0	0	0	0	0	19	0	2	0	0	**39**	**100**
Mannar	0	83	0	6	0	0	0	1	0	0	0	36	1	6	0	1	0	0	0	2	1	9	0	1	**53**	**100**
Vavuniya	1	157	0	10	0	1	0	0	5	23	0	30	0	8	0	2	0	0	1	24	1	13	0	10	**18**	**100**
Mullaitivu	0	118	0	13	0	1	0	4	0	12	0	36	0	6	0	1	0	0	0	17	0	2	0	7	**28**	**100**
Batticaloa	12	2171	5	172	0	8	0	5	0	18	3	85	0	1	0	8	1	3	13	101	2	36	0	1	**67**	**100**
Ampara	5	228	0	9	0	1	0	1	0	53	5	120	0	2	1	2	0	0	1	74	3	51	1	9	**13**	**100**
Trincomalee	8	2007	0	22	0	1	0	1	0	67	2	66	0	15	0	3	0	0	4	67	0	29	2	7	**31**	**100**
Kurunegala	43	2670	3	41	0	15	0	1	0	7	6	347	0	17	1	12	0	2	4	462	7	184	10	473	**30**	**100**
Puttalam	5	2899	1	32	0	3	0	1	0	2	5	83	0	8	0	1	0	0	2	97	2	66	0	19	**29**	**100**
Anuradhapur	7	689	0	13	0	1	0	1	0	8	5	251	1	31	0	4	0	2	0	216	0	43	26	539	**31**	**100**
Polonnaruwa	3	531	0	15	0	6	0	1	0	11	0	156	0	7	0	13	0	0	2	77	1	18	1	361	**37**	**100**
Badulla	25	994	1	37	0	5	0	0	0	44	12	309	2	53	0	83	0	0	12	156	2	45	1	39	**67**	**100**
Monaragala	9	633	1	22	0	6	0	0	0	8	10	472	1	36	0	24	0	1	1	64	3	74	8	162	**31**	**100**
Ratnapura	24	1961	3	45	0	16	0	3	16	48	30	1042	0	27	0	17	0	2	6	189	0	133	8	170	**36**	**100**
Kegalle	24	2726	3	25	0	2	0	2	0	15	11	595	0	42	0	6	0	0	7	396	4	80	1	39	**34**	**100**
Kalmune	6	1694	1	67	0	10	0	0	1	1	2	52	0	1	0	0	0	0	9	125	1	36	0	0	**52**	**100**
SRILANKA	**730**	**62915**	**36**	**947**	**2**	**144**	**1**	**66**	**31**	**558**	**184**	**7259**	**17**	**1099**	**4**	**245**	**1**	**18**	**143**	**4395**	**41**	**1198**	**86**	**2902**	**43**	**99**

Source: Weekly Returns of Communicable Diseases (esurvillance.epid.gov.lk). T=Timeliness refers to returns received on or before 06th Oct, 2023 Total number of reporting units 358 Number of reporting units data provided for the current week: 358 **C****-Completeness

Table 2: Vaccine-Preventable Diseases & AFP

30th– 06th Sep 2023 (40th Week)

Disease	No. of Cases by Province									Number of cases during current week in 2023	Number of cases during same week in 2022	Total number of cases to date in 2023	Total number of cases to date in 2022	Difference between the number of cases to date in 2023 & 2022
	W	C	S	N	E	NW	NC	U	Sab					
AFP*	00	00	01	00	00	00	00	00	00	01	03	73	63	15.8 %
Diphtheria	00	00	00	00	00	00	00	00	00	00	00	00	00	0 %
Mumps	00	03	02	00	01	00	01	00	00	07	02	191	72	165.2 %
Measles	29	07	02	03	00	02	02	01	04	50	02	586	19	2984.2 %
Rubella	00	00	00	00	00	00	00	00	00	00	00	06	00	0 %
CRS**	00	00	00	00	00	00	00	00	00	00	00	02	00	0 %
Tetanus	00	00	00	00	00	00	00	00	00	00	00	06	05	20 %
Neonatal Tetanus	00	00	00	00	00	00	00	00	00	00	00	00	00	0 %
Japanese Enceph-alitis	00	00	00	00	00	00	00	00	00	00	00	02	01	100 %
Whooping Cough	00	00	00	00	00	00	00	00	00	00	00	07	01	600 %
Tuberculosis	67	33	07	04	16	00	12	04	27	170	155	7118	5255	35.4%

Key to Table 1 & 2

Provinces: **W**: Western, **C**: Central, **S**: Southern, **N**: North, **E**: East, **NC**: North Central, **NW**: North Western, **U**: Uva, **Sab**: Sabaragamuwa.

RDHS Divisions: **CB**: Colombo, **GM**: Gampaha, **KL**: Kalutara, **KD**: Kandy, **ML**: Matale, **NE**: Nuwara Eliya, **GL**: Galle, **HB**: Hambantota, **MT**: Matara, **JF**: Jaffna, **KN**: Killinochchi, **MN**: Mannar, **VA**: Vavuniya, **MU**: Mullaitivu, **BT**: Batticaloa, **AM**: Ampara, **TR**: Trincomalee, **KM**: Kalmunai, **KR**: Kurunegala, **PU**: Puttalam, **AP**: Anuradhapura, **PO**: Polonnaruwa, **BD**: Badulla, **MO**: Moneragala, **RP**: Ratnapura, **KG**: Kegalle.

Data Sources:

Weekly Return of Communicable Diseases: Diphtheria, Measles, Tetanus, Neonatal Tetanus, Whooping Cough, Chickenpox, Meningitis, Mumps., Rubella, CRS,

Special Surveillance: AFP* (Acute Flaccid Paralysis), Japanese Encephalitis

CRS =**Congenital Rubella Syndrome

NA = Not Available

Take prophylaxis medications for leptospirosis during the paddy cultivation and harvesting seasons.

It is provided free by the MOH office / Public Health Inspectors.

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ON STATE SERVICE

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