WEEKLY EPIDEMIOLOGICAL REPORT

A publication of the Epidemiology Unit
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WER SRI LANKA 2024

Vol. 51 No. 31 **27th – 02nd Aug 2024**

Vaccine Manufacturing Process II

Organic and Biochemical Manufacturing steps

1. **Bacteria, Virus, or Cell Culture:**

This step involves growing the pathogen or cells in controlled conditions to produce the necessary biological material. The process begins with production of the vaccine's active ingredient, known as the antigen. The antigen is the substance that stimulates an immune response. It can be a virus, bacterium, or toxin. Antigens are selected based on their ability to elicit a robust immune response. The antigen can be derived from various sources, such as inactivated or weakened viruses, proteins, or genetic material. If the vaccine is produced using a cell culture system (e.g., some viral vaccines like the flu vaccine), a master cell bank is established, and cells are grown in bioreactors. The virus or antigen is then propagated in these cells.

2. **Harvesting:**

Once the cells or pathogens have grown to the desired quantity, the next step is harvesting. This involves collecting the cells or viral particles from the culture medium.

3. **Purification:**

The harvested material undergoes purification to remove any unwanted components such as cellular debris and other impurities. Techniques like centrifugation, filtration, and chromatography are commonly used in this step to isolate the desired antigen.

4. **Inactivation (if necessary):**

Inactivation is required for certain vaccines, especially those involving live pathogens. This step ensures that the pathogen can no longer cause disease but still elicits an immune response. Chemical or physical methods can be used for inactivation.

5. **Valence Assembly:**

This step involves combining different antigens if the vaccine is designed to protect against multiple strains or types of pathogens. The goal is to create a multivalent vaccine that provides broader protection.

Pharmaceutical Manufacturing Steps

6. **Formulation:**

The purified antigen is mixed with adjuvants, stabilizers, and other excipients to create the vaccine formulation. These components help enhance the vaccine's efficacy, stability, and shelf life. This process can be complex due to the need to maintain stability and efficacy. Formulation challenges include finding suitable excipients, stabilizers, and adjuvants that preserve the integrity of the vaccine throughout its shelf life. The vaccine formulation is subjected to sterilization methods to eliminate any potential contaminants, such as microorganisms. Common sterilization methods include filtration and heat treatment.

7. **Filling:**

The formulated vaccine is then filled into vials, syringes, or other appropriate containers and is sealed to maintain sterility and accuracy in dose volume. This step must be carried out under sterile conditions to prevent contamination.

8. **Freeze-Drying (if necessary):**

Some vaccines undergo freeze-drying (lyophilization) to improve stability and shelf life. Freeze-dried vaccines need to be reconstituted with a liquid before administration.

9. **Packaging:**

The finished vaccines are packaged into their final presentation forms (e.g., vials, ampules, prefilled syringes). This includes labeling with important information such as batch numbers, expiration dates, and instructions for use.

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10. Batch Release:

Before distribution, each batch of vaccine must pass thorough quality control tests and be reviewed for compliance with regulatory standards. Vaccine manufacturers must submit detailed data and documentation to regulatory authorities for product review and approval. This includes testing for potency, purity, sterility, and safety. Only batches that meet all regulatory standards are released for distribution.

Vaccine manufacturing often involves smaller batch sizes compared to traditional pharmaceuticals. The processes can be more sensitive to variations, requiring careful monitoring and control. Hence, this process is sophisticated and demands specialized equipment and expertise.

11. Distribution:

The final step involves distributing the packaged vaccines to healthcare providers and administering them to individuals as part of vaccination programs. Vaccines are stored and transported in a controlled environment to maintain their stability and potency. Cold chain management is crucial to prevent the degradation of vaccines.

12. Post-Marketing Surveillance:

Post-marketing surveillance is conducted after a vaccine has been approved and involves the frequent evaluation of the safety and effectiveness of the vaccine in a large population. These trials, often called Phase IV clinical trials, are designed to identify rare or long-term side effects that may not have been detected in earlier trials and to ensure that the vaccine remains safe and effective for patients in the real world. Although pre-licensure clinical trials are completed, they have limitations in terms of sample size and duration.

Continuous monitoring of Adverse Events Following Immunization (AEFI) as part of post-marketing surveillance helps identify rare or long-term adverse effects that may only become apparent when the vaccine is administered to a larger, more diverse population. AEFI surveillance involves the systematic collection of data on medically important events following immunization, providing information for investigation and necessary follow-up actions. AEFI surveillance should be part of all immunization programs, and causality assessments of AEFI should be conducted by a national expert committee to help sustain public confidence in the program. The collected and analyzed AEFI data from individual countries is then coordinated and further analyzed by the international expert committee at the global level.

This surveillance helps recognize specific populations or conditions associated with an increased risk of adverse events. Detailed data allows health authorities to tailor recommendations and precautions for vulnerable groups, ensuring personalized and safer vaccination strategies. Insights gained from post-marketing surveillance can lead to significant improvements in vaccine formulation, manufacturing processes, and administration practices, contributing to the development of safer and more effective vaccines over time.

Quality control is an integral part of each step in the vaccine manufacturing process. It involves continuous monitoring and testing to ensure the safety, efficacy, and quality of the vaccine. Regulatory agencies oversee the entire process and require detailed documentation and approval before vaccines can be distributed and administered to the public. Most vaccines produced for the current market undergo the World Health Organization (WHO) pre-qualification process. This process, established by WHO, evaluates both the quality of the vaccine and the manufacturing process, as well as the technical and commercial capabilities of the organization to produce the vaccine. By providing a standard regulatory framework, the WHO pre-qualification process allows manufacturers to obtain approval that is recognized in many countries, eliminating the need for separate regulatory approvals in individual countries.

The vaccine manufacturing process is a highly sophisticated and regulated procedure, involving high manufacturing costs. Factors including the need for specialized facilities, advanced technologies, and extensive quality control, contribute to the overall expense of large molecule vaccine production. The cost of goods for these vaccines can be higher than that of small molecule drugs, as these complexities contribute to increased manufacturing costs.

Despite these challenges, advances in biotechnology and manufacturing technologies are continually improving the efficiency of large-molecule vaccine production. Research and development efforts are focused on addressing these challenges to make the manufacturing process more scalable, cost-effective, and capable of meeting global vaccine demands, especially in the face of emerging infectious diseases.

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Table 1: Selected notifiable diseases reported by Medical Officers of Health 20th – 26th July 2024 (30th Week)

RDHS	Dengue Fever		Dysentery		Encephalitis		En. Fever		F. Poisoning		Leptospirosis		Typhus F.		Viral Hep.		H. Rabiies		Chickenpox		Meningitis		Leishmania-		Tuberculosis		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	A	B	T*	C**
Colombo	321	7082	0	21	0	7	0	45	1	16	13	305	0	8	0	7	0	0	15	322	1	23	0	0	41	1292	**95**	**100**
Gampaha	157	3163	0	27	0	14	1	12	0	70	11	438	1	5	3	5	0	0	9	252	0	79	0	14	0	678	**62**	**100**
Kalutara	65	1912	0	19	0	2	1	29	0	32	16	476	0	5	0	8	0	1	13	408	1	39	0	1	54	361	**100**	**100**
Kandy	120	2899	0	29	0	2	2	8	0	54	3	170	1	22	0	8	0	1	4	289	0	13	4	29	13	347	**96**	**100**
Matale	19	490	1	9	0	0	2	4	0	18	2	70	0	2	0	4	0	0	6	104	0	9	5	174	2	83	**100**	**100**
Nuwara Eliya	5	244	2	99	0	5	0	9	1	195	4	125	0	30	0	5	0	0	3	155	1	11	0	1	3	167	**100**	**100**
Galle	33	1396	0	33	2	20	0	8	2	72	11	486	0	68	0	7	0	1	20	460	2	52	0	3	10	262	**80**	**100**
Hambantota	14	619	1	25	0	3	1	4	1	44	6	330	1	33	0	5	0	1	16	219	0	22	6	318	1	81	**92**	**100**
Matara	44	608	0	7	0	4	0	2	0	26	10	308	5	17	0	3	0	0	10	232	1	60	2	81	1	91	**100**	**100**
Jaffna	10	5147	3	47	0	2	0	22	0	31	0	17	9	426	0	5	0	1	0	150	2	13	0	1	0	180	**100**	**93**
Kilinochchi	1	272	0	9	0	0	0	2	0	2	0	17	1	10	0	0	0	1	1	6	0	5	0	0	2	16	**100**	**100**
Mannar	5	207	1	5	0	0	0	1	0	0	0	21	0	10	0	1	0	0	0	5	0	3	0	1	0	41	**100**	**100**
Vavuniya	5	153	1	10	0	1	0	1	0	21	1	71	0	4	0	4	0	0	1	30	0	13	0	8	0	23	**100**	**100**
Mullaitivu	1	189	0	7	0	0	0	0	0	16	2	62	0	11	0	0	0	0	0	4	0	3	0	8	3	23	**100**	**100**
Batticaloa	15	1249	4	89	0	9	0	6	1	47	3	56	0	2	0	17	0	1	2	84	1	30	0	3	1	97	**93**	**100**
Ampara	5	199	0	26	0	3	0	0	2	17	0	146	0	1	0	5	0	0	1	79	0	28	1	13	2	90	**71**	**100**
Trincomalee	8	572	0	13	0	1	0	3	0	4	0	125	0	12	0	3	0	0	0	43	0	11	1	13	0	74	**100**	**100**
Kurunegala	27	1695	1	34	1	24	0	3	0	345	20	431	0	17	0	4	0	2	12	330	5	184	14	390	8	323	**93**	**100**
Puttalam	24	815	0	5	0	3	0	3	0	3	1	163	2	14	0	1	0	1	3	92	1	45	1	24	5	136	**85**	**100**
Anuradhapura	23	577	0	13	3	6	0	2	0	26	8	306	0	27	0	8	0	1	7	182	8	35	27	555	6	182	**100**	**100**
Polonnaruwa	6	270	0	16	0	0	0	1	0	6	2	199	1	2	11	21	0	0	2	89	1	22	8	334	11	74	**100**	**100**
Badulla	10	624	2	22	1	5	0	4	1	30	10	370	2	23	0	19	0	0	7	239	0	22	2	26	6	144	**100**	**100**
Monaragala	15	556	1	14	1	3	0	2	0	78	12	552	0	23	0	21	0	1	2	77	4	67	6	158	0	72	**100**	**100**
Ratnapura	76	1883	2	73	0	4	0	8	3	15	36	1159	0	16	1	19	0	2	5	213	5	92	2	122	12	197	**80**	**100**
Kegalle	19	1473	0	11	0	6	0	8	0	10	5	452	1	21	0	6	0	1	25	572	0	42	0	19	25	217	**82**	**100**
Kalmunai	3	601	0	15	0	0	0	0	0	5	1	55	1	4	0	4	0	0	1	152	0	11	0	0	0	84	**77**	**100**
SRILANKA	**1031**	**34895**	**19**	**678**	**8**	**124**	**7**	**187**	**12**	**1183**	**177**	**6910**	**25**	**813**	**15**	**190**	**0**	**15**	**165**	**4788**	**33**	**934**	**79**	**2296**	**206**	**5269**	**93**	**99**

Source: Weekly Returns of Communicable Diseases (esurvillance.epid.gov.lk). T=Timeliness refers to returns received on or before 26th July, 2024 Total number of reporting units 358 Number of reporting units data provided for the current week: 358**C****-Completeness *

A = Cases reported during the current week. B = Cumulative cases for the year.

Table 2: Vaccine-Preventable Diseases & AFP

20th – 26th July 2024 (30th Week)

Disease	No. of Cases by Province									Number of cases during current week in 2024	Number of cases during same week in 2023	Total number of cases to date in 2024	Total number of cases to date in 2023	Difference between the number of cases to date in 2024 & 2023
	W	C	S	N	E	NW	NC	U	Sab					
AFP*	00	01	00	00	00	00	00	00	00	01	04	41	54	-24 %
Diphtheria	00	00	00	00	00	00	00	00	00	00	00	00	00	0 %
Mumps	01	00	01	00	00	00	01	00	01	04	04	166	131	26.7 %
Measles	00	00	03	00	00	02	00	00	00	05	45	232	140	65.7.2 %
Rubella	00	00	00	00	00	00	00	00	00	00	00	02	01	100 %
CRS**	00	00	00	00	00	00	00	00	00	00	00	00	00	0 %
Tetanus	00	00	00	00	00	00	00	00	00	00	00	04	06	-33.3 %
Neonatal Tetanus	00	00	00	00	00	00	00	00	00	00	00	00	00	0 %
Japanese Encephalitis	00	00	00	00	00	00	00	00	00	00	00	06	02	200 %
Whooping Cough	00	00	00	00	00	00	01	00	01	02	00	36	05	620 %

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.

Comments and contributions for publication in the WER Sri Lanka are welcome. However, the editor reserves the right to accept or reject items for publication. All correspondence should be mailed to The Editor, WER Sri Lanka, Epidemiological Unit, P.O. Box 1567, Colombo or sent by E-mail to **chepid@sltnet.lk. Prior approval should be obtained from the Epidemiology Unit before publishing data in this publication**

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