

Indian Type O/A/Asia-1 vaccine strains recommendation for Iran.

FMD virus (FMDV) epidemiology in Iran.

FMD in Iran countries is sporadic and intermediate and most FMD outbreaks in Iran have been caused by serotype O, serotype A and Asia 1. As per the World Reference Laboratory for FMD (WRL FMD) Iran countries is coming under pool 3 named as West Eurasia & Middle east (**Figure 1**).

<u>Serotype</u>	<u>Years</u>
Type O	1956, 1958-1964, 1966, 1987, 1993-2007, 2009-2018.
Type A	1960-1962, 1965-1966, 1987, 1993-2018.
Type Asia 1	1957, 1964, 1973, 1999, 2001, 2004, 2011-2013, 2015-2016, 2018.
SaT-1	1962-1964

Table 1: FMDV Outbreaks in Iran.

POOL	REGION/COUNTRIES – colour pools as in Map	SEROTYPES
1	SOUTHEAST ASIA/CENTRAL ASIA/EAST ASIA Cambodia, China (People's Rep. of), China (Hong Kong, SAR), China (Taiwan Province), Korea (DPR), Korea (Rep. of), Laos PDR, Malaysia, Mongolia, Myanmar, Russian Federation, Thailand, Viet Nam	O, A and Asia 1
2	SOUTH ASIA Bangladesh, Bhutan, India, Nepal, Sri Lanka	O, A and Asia 1
3	WEST EURASIA & MIDDLE EAST Afghanistan, Algeria, Armenia, Azerbaijan, Bahrain, Bulgaria, Egypt , Georgia, Iran, Iraq, Israel, Jordan, Kazakhstan, Kuwait, Kyrgyzstan, Lebanon, Libya , Morocco, Oman, Pakistan, Palestine, Qatar, Saudi Arabia, Syrian Arab Republic, Tajikistan, Tunisia, Turkey, Turkmenistan, United Arab Emirates, Uzbekistan	O, A and Asia 1
4	EASTERN AFRICA Burundi, Comoros, Congo D. R. , Djibouti, Egypt , Eritrea, Ethiopia, Kenya, Libya , Rwanda, Somalia, Sudan, South Sudan, Tanzania, Uganda, Yemen	O, A, SAT 1, SAT 2 and SAT 3
5	WEST/CENTRAL AFRICA Benin, Burkina Faso, Cameroon, Cape Verde, Central Afr. Rep., Chad, Congo D. R. , Congo, Côte d'Ivoire, Equatorial Guinea, Gabon, Gambia, Ghana, Guinea Biss., Guinea, Liberia, Mali, Mauritania, Niger, Nigeria, Sao Tome Principe, Senegal, Sierra Leone, Togo	O, A, SAT 1 and SAT 2
6	SOUTHERN AFRICA Angola, Botswana, Congo D. R. , Malawi, Mozambique, Namibia, South Africa, Zambia, Zimbabwe	{O, A}*, SAT 1, SAT 2 and SAT 3
7	SOUTH AMERICA Ecuador, Paraguay, Venezuela	O and A

Egypt, Libya and Congo D. R. (highlighted in bold) are indicated as being in multiple pools, since they have evidence of FMDV originating from 2 or more pools in the past four years. * ONLY IN NORTH ZAMBIA AS SPILL-OVER FROM POOL 4

Figure 1: Distribution of the seven endemic pools of FMD showing the predominant viral serotypes that are present in each region, as well as the conjectured status of FMD in countries.

S. No	Serotypes	Topotype	Lineage	Sub-lineage
1	Type O	ME-SA	PanAsia-2	Far-09 Bal-09 Qom-15 Ant-10
2	Type A	ASIA	GVII Iran-05	- Sis-10 Sis-12 Sis-13 Her-10
3	Type Asia 1	ASIA	Sindh-08	-

Table 2: Predominant FMDV types causing recent outbreaks in Iran
(http://www.wrlfmd.org/fmd_genotyping/me/irn.htm)

Genotypic Matching of Type O Iran outbreak strains with Indian vaccine strain (O/IND/R2/75)

As per WRL FMD Molecular Epidemiology Reports O/IND/R2/75 strain is closely related reference virus as it shows 88.42- 89.67 % identity with type O field isolates from Iran.

Sl. No	Name of epizootic type "O" FMDV strains	Name of RakshaOvac TV™ vaccine type "O" FMDV strain	Degree of genetic relationship FMDV strains%	
			Identity (%)	Reference
1	IRN/29/2006	O/IND/R2/75 (AF204276)	89.67	WRLFMD/2006/00036
2	IRN/26/2007	O/IND/R2/75 (AF204276)	88.58	WRLFMD/2007/00156
3	IRN/7/2009	O/IND/R2/75 (AF204276)	87.64	WRLFMD/2009/00007
4	IRN/33/2010	O/IND/R2/75 (AF204276)	88.42	WRLFMD/2010/00018

The current Indian serotype O vaccine strain O/IND/R2/75 is a good match with the circulating field isolates in India and with the majority of the field isolates studied from other Asian countries(1). A study by Mahapatra M., et al. shown antigenic relationship with Indian vaccine strain (O/IND/R2/75) with ME-SA (PanAsia) topotype. Among the viruses used 89.29% of it shown closer antigenic relationship with above 0.3 r-value. In Iran where type O outbreaks where predominantly caused by ME-SA- PanAsia topotypes can be counteracted with Indian type O (O/IND/R2/75) vaccine strain.

Vaccine/topotype	O/PanAsia-2	O/HKN/6/83	O/MYA/2009	O/SKR/2010	O/IND/R2/75
ME-SA (PanAsia)	96.43	85.71	75.00	46.43	89.29
ME-SA (Ind-2001d)	100	75	12.5	25.00	100
SEA (Mya-98)	94.23	94.23	96.15	69.23	78.85
Cathay	100	100	100	20	40
Total	95.29	91.76	89.41	58.82	80.00

Table 3: Indian vaccine strain (O/IND/R2/75) (Bolted red) exhibiting antigenic relationship (r_1) values above 0.3 (good match) against viruses of different topotypes of which it shows 89.29% matching with ME-SA (PanAsia) topotype (Mahapatra M., et al. Vaccine. 2017 Dec 18; 35(51): 7147–7153.)

Genotypic Matching of Type A Iran outbreak strains with Indian vaccine strain (A/IND/40/2000)

As per WRL FMD Molecular Epidemiology Reports A/IND/40/2000 strain is closely related reference virus as it shows 89.67- 90.6% identity with type A field isolates from Iran.

Sl. No	Name of epizootic type “A” FMDV strains	Name of RakshaOvac TV TM vaccine type “A” FMDV strain	Degree of genetic relationship FMDV strains%	
			Identity (%)	Reference
1	IRN/8/2015	IND/40/2000	89.67	WRLFMD/2015/00031
2	IRN/8/2015	IND/40/2000	89.98	WRLFMD/2015/00031
3	IRN/11/2016	IND/40/2000	90.0	WRLFMD/2016/00018
4	IRN/12/2016	IND/40/2000	90.3	WRLFMD/2016/00018
5	IRN/20/2016	IND/40/2000	90.4	WRLFMD/2016/00018
6	IRN/23/2016	IND/40/2000	90.4	WRLFMD/2016/00018
7	IRN/8/2016	IND/40/2000	90.0	WRLFMD/2016/00018
8	IRN/1/2016	IND/40/2000	90.1	WRLFMD/2016/00018
9	IRN/39/2016	IND/40/2000	90.2	WRLFMD/2017/00008
10	IRN/4/2017	IND/40/2000	90.3	WRLFMD/2017/00008
11	IRN/25/2018	IND/40/2000	90.6	WRLFMD/2018/00007
12	IRN/9/2018	IND/40/2000	90.6	WRLFMD/2018/00007

Genotypic Matching of Type Asia-1 Iran outbreak strains with Indian vaccine strain (As1/IND/63/72)

As per WRL FMD Molecular Epidemiology Reports As1/IND/63/72 strain is closely related reference virus as it shows 83.7- 84.76% identity with type Asia1 field isolates from Iran.

Sl. No	Name of epizootic type “Asia1” FMDV strains	Name of RakshaOvac TV™ vaccine type “Asia-1” FMDV strain	Degree of genetic relationship FMDV strains%	
			Identity (%)	Reference
1	IRN/33/2011	Asia1/IND/63/72 (AY304994)	84.76	WRLFMD/2011/00020
2	IRN/38/2011	Asia1/IND/63/72 (AY304994)	84.76	WRLFMD/2011/00020
3	IRN/14/2012	Asia1/IND/63/72 (AY304994)	84.04	WRLFMD/2012/00027
4	IRN/15/2013	Asia1/IND/63/72 (AY304994)	84.13	WRLFMD/2014/00006
5	IRN/1/2015	Asia1/IND/63/72 (AY304994)	84.24	WRLFMD/2015/00031
6	IRN/26/2016	Asia1/IND/63/72 (AY304994)	83.7	WRLFMD/2016/00018
7	IRN/7/2018	Asia1/IND/63/72 (AY304994)	84.7	WRLFMD/2018/00007
8	IRN/17/2018	Asia1/IND/63/72 (AY304994)	83.9	WRLFMD/2018/00007
9	IRN/19/2018	Asia1/IND/63/72 (AY304994)	84.3	WRLFMD/2018/00007

Information of RakshaOvac TV:

Raksha–Ovac Trivalent (FMD Oil Adjuvant vaccine) is a unique Double Emulsion Oil Adjuvant Vaccine and is recommended for prophylactic vaccination against Foot and Mouth Disease in cattle, buffaloes, sheep, goats and pigs. RakshaOvac Trivalent FMD Oil Adjuvant vaccine contains tissue culture virus strains “O, A and Asia1” and inactivated with Aziridine compound. Mineral oil is added as an adjuvant. Thiomersal 0.01% w/v added as preservative. Tailor made individual serotype vaccine are also available based customer requirements.

FMD NSP free status of RakshaOvac TV™ vaccine:

The Project Directorate on FMD (Indian Council of Agricultural Research; ICAR) has shown that FMD vaccine from IIL did not elicit any FMD NSP antibody response in vaccinated animal (Mohapatra et al, 2011).

Summary:

In summary genotype match analysis of Indian type O vaccine strain with type O field isolates of Iran shows 88.42- 89.67 % identity. The major type O topotypes found in Iran are ME-SA topotypes PanAsia lineage. Based on WRL- FMD (Pirbright) vaccine matching study reports which includes Indian vaccine strain (O/IND /R2/72) shows that it

cross reacts with ME-SA topotypes PanAsia lineage strains of with r-value of above 0.3 which means they can be protected by Indian type O vaccine strain. In case of type A the genotypic match analysis of Indian type A vaccine strain with type A field isolates of Iran shows 89.67- 90.6% percent identity. In case of type Asia-1 the genotypic match analysis of Indian type Asia-1 vaccine strain with type Asia-1 field isolates of Iran shows 83.7- 84.76 % percent identity. Based on the above data we believe that RakshaOvac TV™ vaccine is compatible with field FMDV virus in the territory of Iran and may be used for prevention and animal epidemic counter measures for FMDV liquidation.

References:

1. Mahapatra M, *et al.* Antigenic and genetic comparison of foot-and-mouth disease virus serotype O Indian vaccine strain, O/IND/R2/75 against currently circulating viruses. *Vaccine*. 2015 Jan 29; 33(5):693-700.
2. Mahapatra M, *et al.* Selection of vaccine strains for serotype O foot-and-mouth disease viruses (2007–2012) circulating in Southeast Asia, East Asia and Far East. *Vaccine* 35 (2017) 7147–7153.
3. OIE/FAO Foot-and-Mouth Disease Reference Laboratory Network, Annual report 2016.
4. http://www.wrlfmd.org/fmd_genotyping/me/irn.htm