



Data Article

Toxicological data of rats and rabbits: Sub-chronic testing of recombinant HPV vaccine through oral and intranasal routes



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ABSTRACT

Current article illustrates the data of body weight, biochemical, haematological profile, and organ weights of rats and rabbits administered with recombinant human papilloma virus (HPV) vaccine, along with genotoxicity effect. The data was collected from nonclinical safety/toxicity and immune response evaluations of recombinant *Salmonella typhi* expressing the HPV 16 and 18 L1 proteins as vaccine. The intended clinical route of vaccine administration is through oral route, whereas it is established fact that attenuated *S. typhi* could not colonize in laboratory animals. In view of this it is challenging to undertake the nonclinical safety/toxicity evaluations following the regulatory guidelines. Hence sub chronic safety/toxicity testing was carried out in rat and rabbits by administration of HPV vaccine through oral (intended clinical route) and innovative intranasal routes.

The prophylactic dose derived from adult human clinical dose (2×10^9 CFU/70 kg) was administered to SD rats (PD: 0.18×10^9 CFU/kg) and New Zealand White (NZW) rabbits

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(PD: 0.09×10^9 CFU/kg) through oral and intranasal routes. Similarly, average dose (AD:5xPD) was administered to rats (AD: 0.9×10^9 CFU/kg) and rabbits (AD: 0.45×10^9 CFU/kg) through intranasal route only. The repeated doses were administered on 3rd and 5th days of post-exposure of 1st dose through specified routes and test compound effects in relation with time of exposure was assessed by euthanizing animals and data collection at different time points i.e. 15th (25% of animals), 29th (25% of animals) and 93rd days (50% of animals) of post-exposure of 1st dose. The retro-orbital plexus blood was collected before euthanizing animals to unveil the biochemical and haematological profile. The data on genotoxicity effect of test compound, if any, was obtained by assessing the bone-marrow micronucleus assay. The immune response and allergenicity in terms of specific IgG and IgE levels against HPV 16 and 18 L1 proteins were determined in mice. The raw data of various parameters collected at different time points were compiled and computed according to the groups. The haematological profile and organ weights data can be used as reference data for SD rats and NZW rabbits for future studies.

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Specifications Table

Subject	Pharmacology, Toxicology and Pharmaceuticals Science
Specific subject area	Sub chronic Toxicity Testing of HPV 16 & 18 L1 Expressing <i>S. typhi</i>
Type of data	Tables
How data were acquired	Rats and rabbits were administered with prophylactic dose (PD) and average dose (5xPD) of recombinant <i>S. typhi</i> expressing HPV 16 & 18 L1 proteins through oral and intranasal routes. Repeated exposure effect of test compound was assessed by administration of HPV vaccine on 3rd and 5th day through the specified routes. Test compound effects on route and dose of administration was assessed in blood and recording vital organ weights after euthanizing animals at different time points.
data format	analysed data of mean and sd
Parameters for data collection	Haematological profile was collected using automated blood cell counter as per the manufacturer's instructions and guidelines (Serono Baker System 9120 CP+, USA). The organ weights were recorded on weighing balance (Sartorius, SECURA125-1OBR).
Description of data collection	Data was compiled and computed to derive mean and standard deviation (SD) using SPSS 15.0 windows version. Blood was collected from retro-orbital plexus using microhematocrit capillaries (Fisher Scientific # 22-362,566) into K2EDTA tubes (BD Vacutainer). Haematological investigations includes total white blood cell (WBC) count, red blood cell (RBC) count, haemoglobin (Hb), haematocrit (HCT), mean corpuscular volume (MCV), mean corpuscular haemoglobin (MCH), mean corpuscular haemoglobin concentration (MCHC), platelet count, mean platelet volume (MPV) and differential leucocytes counts. The data collected from all the animals of each and every group was compiled and computed.

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Data source location	Department: Advanced Centre for Preclinical Toxicology Studies Institution: ICMR – National Institute of Nutrition City/Town/Region: Hyderabad, Telangana Country: India
Data accessibility	With the article
Related research article	Srinivasa Reddy Y, Narendra Babu K, Uday Kumar P, Harishankar N, Qadri SSYH, Surekha MV, Hemalatha R, Dinesh Kumar B. Nonclinical Safety Evaluation of Oral Recombinant Anti-Human Papilloma Virus Vaccine (RHPV 16 & 18): Regulatory Toxicology Studies In Mice, Rats And Rabbits - An Innovative Approach. <i>Vaccine</i> 39 (2021) 853–863. https://doi.org/10.1016/j.vaccine.2020.11.023

Value of the Data

- The data of current report is extremely useful as it obtained from rats and rabbits administered with attenuated *S. typhi* Ty21a expressing HPV 16 & 18 L1 Protein as vaccine candidate.
- Further, the haematological profile data is useful as it was collected from laboratory animals exposed to HPV Vaccine through intended clinical oral and innovative intranasal routes.
- The data of vital organ weights of rats and rabbits is used as reference data.
- This data helps the pharmacologists, regulatory agencies and policy makers to consider the alternate and innovative methods of ‘New Drug Testing’ procedures.

1. Data Description

The data of current article describes about various parameters analysed as body weights, biochemical, haematological profile in blood samples and organ weights along with genotoxicity effect, collected from rats and rabbits administered the recombinant *S. typhi* TY21a HPV (rSt.HPV) expressing HPV 16 and 18 L1 proteins as vaccine through oral and intranasal routes. Blood was collected before euthanizing at different time points (post-exposure of 1st dose) after three successive dosing of HPV vaccine, at the same time points vital organs were collected and recorded the weights after euthanizing the animals. The raw data from all the animals of different groups were compiled and computed accordingly.

Data of [Table 1](#) comprises of body weights of rats used for sub-chronic toxicity study testing of the rSt.HPV expressing 16 and 18 L1 proteins.

Data of [Table 2](#) comprised of body weights of rabbits used to test the sub-chronic toxicity of rSt.HPV expressing 16 and 18 L1 proteins.

Data of [Tables 3.1–3.3](#) consists of haematological profile of rats euthanized on 15th, 29th and 93rd day of post-exposure of 1st dose administration of HPV vaccine as part of sub-chronic testing. The haematological profile includes haemoglobin, red blood cells (RBC), white blood cells (WBC), haematocrit (HCT), mean corpuscular volume (MCV), and mean corpuscular haemoglobin (MCH), mean corpuscular haemoglobin concentration (MCHC), platelets, neutrophils, lymphocytes, monocytes, eosinophils from rats.

Similarly, the haematological profile of rabbits euthanized on 15th, 29th and 93rd days of post-administration of 1st dose of recombinant HPV vaccine were given in [Tables 4.1–4.3](#), respectively.

Data of [Table 5](#) comprised of biochemical profile of rats used for subchronic testing of rSt.HPV expressing HPV 16 and 18 L1 proteins. The biochemical profile includes ALT, AST, ALP, creatinine, total bilirubin, urea, glucose, calcium, total protein and albumin levels. Similarly, the [Table 6](#) composed of biochemical profile of rabbits administered with rSt.HPV expressing HPV 16 and 18 L1 proteins as part of subchronic testing.

The data on weights of vital organs viz. brain, heart, kidneys, liver, lung, spleen and testis of rats euthanized on 15th, 29th and 93rd days were given in [Tables 7.1–7.3](#).

Similarly, the data on weights of vital organs of rabbits administered with HPV vaccine euthanized on 15th day, 29th day and 93rd day were given in [Tables 8.1–8.3](#).

Table 1
Body weights (g) of rats used for sub-chronic toxicity testing.

	Sex	Baseline	8th Day	16th Day	22nd Day	29th Day	43rd Day	57th Day	71st Day	89th Day	
Vehicle Control (VC)	♂	182.10	208.00	Euthanized on 15th Day							
		216.60	234.60								
		218.30	235.50								
		191.50	210.00	237.20	240.30	Euthanized on 29th Day					
		238.60	258.30	264.50	278.70						
		224.20	247.70	269.30	277.50						
		202.70	238.00	262.60	267.50	314.40	362.20	391.50	405.40	419.00	
		196.80	189.00	223.90	235.20	266.50	308.90	329.60	342.10	367.00	
		213.60	225.60	255.30	257.60	284.50	317.50	333.90	346.70	336.00	
		207.90	211.20	209.80	208.60	241.30	282.70	310.30	319.30	335.00	
	231.30	243.10	237.90	236.70	275.20	306.90	352.70	373.20	381.00		
	239.20	231.50	236.50	240.30	261.60	322.80	338.60	350.90	360.00		
	199.20	208.30	Euthanized on 15th Day								
	212.40	207.40									
	199.20	210.60									
	182.50	199.90	217.40	195.50	Euthanized on 29th Day						
	196.70	215.30	210.50	197.70							
	193.70	179.80	184.80	169.20							
	191.90	207.30	206.90	192.30	216.20	215.60	223.80	233.20	224.00		
	200.10	218.80	209.60	188.70	229.60	236.90	242.60	256.50	251.00		
197.10	203.30	196.80	205.80	213.50	227.50	237.50	248.30	252.00			
192.90	226.00	237.40	215.80	235.50	236.30	255.40	275.10	250.00			
191.00	200.60	203.90	171.80	196.60	215.90	244.30	259.20	253.00			
208.10	228.50	236.30	207.60	238.50	243.50	261.50	291.90	268.00			

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Table 1 (continued)

	Sex	Baseline	8th Day	16th Day	22nd Day	29th Day	43rd Day	57th Day	71st Day	89th Day	
Experimental Control - Intra-Nasal (EC-IN)	♂	208.60	223.50	Euthanized on 15th Day							
		217.20	255.40								
		225.10	244.70								
		175.90	196.80	206.40	210.30	Euthanized on 29th Day					
		216.40	208.40	237.60	239.60						
		189.90	215.30	243.80	237.70						
		200.70	232.50	265.70	256.80	294.60	332.10	348.30	358.70	354.00	
		217.10	249.60	277.40	258.90	276.30	287.60	347.50	359.90	387.00	
		199.40	209.80	237.20	250.60	278.60	288.70	334.40	348.20	352.00	
		229.60	232.60	237.80	229.80	268.50	320.80	354.20	366.20	371.00	
	232.30	250.70	251.40	242.50	273.60	313.70	351.30	361.20	378.00		
	276.40	285.60	273.20	263.40	299.90	356.40	392.10	406.90	410.00		
	♀	205.10	204.60	Euthanized on 15th Day							
		183.30	191.30								
		204.10	199.20								
		189.70	201.60	208.90	209.60	Euthanized on 29th Day					
		187.60	187.80	200.80	202.20						
		201.00	219.60	234.40	240.70						
		199.40	211.30	201.40	210.90	227.00	239.10	245.20	255.30	253.00	
		203.20	223.40	213.40	213.60	233.80	246.80	248.30	262.10	248.00	
199.90		203.50	196.30	204.50	231.80	233.40	250.50	258.90	256.00		
201.50		190.30	207.50	214.60	217.50	226.10	233.40	243.20	230.00		
203.40	206.30	231.50	236.10	241.30	253.40	262.40	272.60	275.00			

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Table 1 (continued)

	Sex	Baseline	8th Day	16th Day	22nd Day	29th Day	43rd Day	57th Day	71st Day	89th Day
Experimental Control - Oral (EC-OR)	♂	212.30	248.60	Euthanized on 15th Day						
		202.80	216.60							
		205.10	231.30							
		203.30	216.70	258.20	236.90	Euthanized on 29th Day				
		204.10	188.70	228.90	237.70					
		249.40	276.60	283.90	265.20					
		191.10	222.60	256.40	238.80	290.20	334.70	363.20	372.80	396.00
		209.70	244.20	260.40	245.50	280.30	336.50	362.10	374.70	383.00
		255.50	273.60	290.30	287.60	322.90	358.90	385.70	400.00	417.00
		210.10	212.50	222.80	219.50	240.50	287.30	322.30	345.20	364.00
	254.10	279.00	286.30	265.40	303.50	351.70	382.70	401.20	411.00	
	238.50	261.30	282.90	267.30	307.90	364.20	396.30	408.90	419.00	
	200.80	226.60	Euthanized on 15th Day							
	236.80	240.40								
	205.20	222.10								
	190.20	199.80	184.60	177.80	Euthanized on 29th Day					
	183.50	199.50	199.80	195.30						
	208.90	221.90	233.00	232.40						
	183.50	200.10	203.70	199.90	216.20	228.70	230.80	254.70	244.00	
	199.70	197.40	225.20	209.60	229.30	234.60	243.10	270.10	265.00	
189.80	185.70	207.90	196.40	220.80	235.80	233.20	253.20	245.00		
198.60	196.60	216.70	200.70	221.20	227.70	234.10	255.50	246.00		
218.40	238.20	260.90	273.30	254.60	253.40	263.90	283.90	278.00		
205.60	215.70	229.70	225.60	230.00	233.20	238.50	251.40	256.00		

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Table 1 (continued)

	Sex	Baseline	8th Day	16th Day	22nd Day	29th Day	43rd Day	57th Day	71st Day	89th Day	
Prophylactic Dose – Intra-Nasal (PD-IN)	♂	207.30	216.90	Euthanized on 15th Day							
		204.80	226.10								
		222.10	236.50								
		193.30	199.60	207.50	213.20	Euthanized on 29th Day					
		253.60	278.40	296.50	305.20						
		268.70	295.30	320.90	326.70						
		186.40	190.80	195.60	197.20	241.90	305.30	330.30	358.20	380.00	
	229.00	257.80	262.90	260.40	296.60	335.20	373.20	391.30	400.00		
	201.40	215.80	244.40	247.40	279.50	305.80	339.40	354.20	368.00		
	230.50	249.60	264.80	264.90	291.20	314.20	340.50	354.50	363.00		
	202.30	228.40	261.60	278.10	310.50	349.20	369.10	385.80	402.00		
	229.80	247.60	264.40	275.50	303.70	334.50	362.30	365.70	376.00		
	♀	195.30	198.70	Euthanized on 15th Day							
		186.90	188.80								
	215.30	226.60									
	186.10	198.30	215.50	224.80	Euthanized on 29th Day						
	192.70	203.50	213.60	223.40							
	200.70	209.60	224.10	224.20							
	192.50	210.00	226.10	234.20	235.30	246.20	278.50	275.70	274.00		
	195.40	215.30	224.10	230.50	238.70	214.40	241.90	262.30	258.00		
	180.40	196.60	216.40	230.20	232.30	255.80	264.30	275.80	271.00		
	222.10	223.00	226.20	221.20	239.80	241.90	254.70	271.00	262.00		

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Table 1 (continued)

	Sex	Baseline	8th Day	16th Day	22nd Day	29th Day	43rd Day	57th Day	71st Day	89th Day	
Prophylactic Dose – Oral (PD-OR)	♂	183.80	225.80	Euthanized on 15th Day							
		217.60	255.30								
		254.70	256.80								
		206.90	229.20	252.80	269.30	Euthanized on 29th Day					
		195.70	215.90	219.80	229.50						
		202.30	231.30	264.60	263.90						
		170.60	202.50	230.70	246.70	266.40	304.80	329.80	343.80	355.00	
		262.90	296.50	303.80	321.20	370.50	417.70	448.30	455.70	471.00	
		217.90	235.60	227.60	230.40	265.50	302.30	332.80	338.90	344.00	
		186.20	219.50	236.10	233.40	246.30	270.80	291.50	292.30	297.00	
	228.70	235.60	244.80	247.20	268.20	275.60	298.80	306.30	321.00		
	236.80	243.70	259.00	266.10	293.20	329.80	363.20	373.50	396.00		
	189.60	200.10	Euthanized on 15th Day								
	210.70	234.30									
	222.80	224.80									
	174.80	207.30	203.80	203.50	Euthanized on 29th Day						
	209.40	215.40	220.30	208.50							
	231.60	215.50	223.20	227.70							
	214.20	217.80	224.20	233.20	234.90	228.30	235.60	249.20	241.00		
	197.80	215.30	211.70	206.60	231.40	238.90	242.40	265.30	255.00		
201.70	209.80	200.30	190.50	221.60	226.70	233.60	249.00	249.00			
212.60	225.70	221.80	210.90	239.90	251.90	254.70	271.30	288.00			
207.40	216.00	218.90	208.50	224.50	236.20	240.40	253.70	259.00			
216.80	220.10	230.90	228.80	241.60	245.10	246.50	262.80	252.00			

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Table 1 (continued)

	Sex	Baseline	8th Day	16th Day	22nd Day	29th Day	43rd Day	57th Day	71st Day	89th Day
Average Dose – Intra-Nasal (AD-IN)	♂	201.40	197.30	Euthanized on 15th Day						
		201.00	248.70							
		286.10	298.90							
		226.20	255.50	283.20	278.80	Euthanized on 29th Day				
		201.00	226.80	246.50	238.80					
		221.40	223.50	251.70	263.40					
		212.30	226.80	247.80	241.50	277.50	317.40	339.40	343.10	333.00
		221.00	239.30	244.20	242.60	292.60	364.30	403.80	435.20	461.00
		198.60	228.80	250.50	264.10	277.80	316.20	347.60	351.20	364.00
		208.60	244.30	270.10	259.50	313.20	321.60	389.20	405.30	412.00
	214.40	230.60	245.20	236.80	278.20	360.10	347.80	359.70	360.00	
	236.10	240.00	271.00	283.10	298.30	321.20	345.90	364.30	375.00	
	203.20	216.30	Euthanized on 15th Day							
	197.40	207.40								
	194.20	136.80								
	180.70	201.30	210.80	217.80	Euthanized on 29th Day					
	193.70	191.80	224.50	214.50						
	183.60	170.80	182.00	187.60						
	190.20	205.50	216.30	220.20	223.70	230.00	240.70	249.30	241.00	
	208.20	211.10	228.80	173.50	231.20	244.10	284.70	287.10	283.00	
226.80	237.80	242.50	182.20	240.50	242.70	296.60	308.20	308.00		
193.50	155.60	183.50	185.90	209.50	215.30	227.50	238.10	231.00		
195.30	175.90	207.20	200.70	232.50	248.30	258.40	272.90	280.00		
187.90	165.70	169.30	190.50	219.50	233.70	236.80	254.80	253.00		

Table 2
Body weights (g) of rabbits used for sub-chronic toxicity testing.

	Sex	Baseline	8th Day	19th Day	26nd Day	37th Day	50th Day	64th Day	78th Day	89th Day
Vehicle Control (VC)	♂	1520.0	1714.0	Euthanized on 15th Day						
		1870.0	1979.0							
		1970.0	2008.0							
		1502.0	1577.0	1560.0	1502.0	Euthanized on 29th Day				
		2238.0	2417.0	2630.0	2741.0					
		1621.0	1690.0	1740.0	1767.0	1773.0	1793.0	1787.0	1784.0	1797.5
		1675.0	1778.0	1869.0	1866.0	1835.0	1900.0	1937.0	1962.0	1956.2
		1970.0	2174.0	2219.0	2195.1	2214.0	2271.0	2349.0	2360.0	2292.0
		2040.0	2353.0	2544.0	2723.0	2706.0	2762.0	2878.0	2823.0	2555.0
		2261.0	2475.0	2537.0	2508.0	2618.0	2663.0	2443.0	2430.0	2440.6
	♀	1884.0	1888.0	Euthanized on 15th Day						
		2399.0	2486.2							
		1778.0	2033.4	2102.5	2305.5	Euthanized on 29th Day				
		1768.0	1881.8	1939.3	2046.6					
		2100.0	2223.4	2426.0	2473.1					
		1917.0	1999.4	2333.0	2354.0	2365.4	2481.0	2530.0	2597.0	2616.4
		2086.0	2194.3	2553.0	2682.7	2579.0	2599.0	2690.0	2740.0	2539.0
		2184.0	2333.2	2673.0	2723.3	2722.0	2745.0	2869.0	2881.0	2848.7
		1967.0	2095.4	2226.0	2344.3	2340.0	2406.0	2497.0	2477.0	2544.0
		2168.0	2335.6	2521.0	2532.7	2525.0	2562.0	2709.0	2702.0	2674.5

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Table 2 (continued)

	Sex	Baseline	8th Day	19th Day	26nd Day	37th Day	50th Day	64th Day	78th Day	89th Day	
Experimental Control Intra-Nasal (EC-IN)	♂	1320.0	1466.0	Euthanized on 15th Day							
		1581.0	1269.0								
		2260.0	2429.0								
		2125.0	2322.0	2513.0	2630.0	Euthanized on 29th Day					
		1826.0	1883.0	2057.0	2085.0						
		2051.0	2185.0	2255.0	2353.0	2440.0	2360.0	2510.0	2454.0	2474.2	
		1970.0	2158.0	2400.0	2448.0	2501.0	2470.0	2437.0	2460.0	2518.0	
		2066.0	2226.0	2369.0	2414.0	2439.0	2486.0	2528.0	2487.0	2540.0	
		2208.0	2381.0	2690.0	2812.0	2802.0	2815.0	2893.0	2905.0	2954.0	
	♀	2232.0	2353.0	2502.0	2604.0	2635.0	2674.0	2680.0	2598.0	2674.2	
		1810.0	1852.0	Euthanized on 15th Day							
		2206.0	2364.2								
		1711.0	1756.0	1897.0	1924.8	Euthanized on 29th Day					
		2098.0	2205.0	2398.0	2338.7						
		2097.0	2211.6	2485.0	2512.0						
		2045.0	2281.2	2626.0	2701.3	2770.0	2889.0	3012.0	2934.0	2577.0	
		1901.0	2037.3	2293.0	2329.7	2410.0	2349.0	2547.0	2540.0	2557.0	
		1845.0	1980.0	2129.0	2257.6	2129.0	2253.0	2339.0	2409.0	2431.0	
		2032.0	2086.2	2271.0	2236.9	2329.0	2305.0	2394.0	2465.0	2494.4	
2294.0	2424.7	2648.0	2710.2	2796.0	2839.0	2937.0	2953.0	2928.2			

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Table 2 (continued)

	Sex	Baseline	8th Day	19th Day	26nd Day	37th Day	50th Day	64th Day	78th Day	89th Day
Experimental Control Oral (EC-OR)	♂	1765.0	1949.0	Euthanized on 15th Day						
		1415.0	1472.0							
		1908.0	2075.0							
		1955.0	2076.0	2227.0	2261.0	Euthanized on 29th Day				
		1830.0	1862.0	2010.0	2017.0					
		2158.0	2285.0	2515.0	2512.0	2464.0	2455.0	2497.0	2416.0	2249.0
		2020.0	2203.0	2237.0	2343.0	2300.0	2248.0	2299.0	2207.0	2155.0
		2093.0	2239.0	2299.0	2353.0	2329.0	2327.0	2424.0	2425.0	2325.0
		2165.0	2329.0	2529.0	2512.0	2479.0	2546.0	2637.0	2612.0	2699.0
	2291.0	2349.0	2535.0	2550.0	2351.0	2374.0	2298.0	2410.0	2465.5	
	2078.0	2162.3	Euthanized on 15th Day							
	2431.0	2579.7								
	1900.0	2040.8	2254.0	2342.3	Euthanized on 29th Day					
	2242.0	2363.2	2699.0	2816.0						
	1849.0	1953.2	2130.0	2220.1						
	1948.0	2059.1	2361.0	2414.0	2496.0	2570.0	2670.0	2677.0	2763.0	
	1945.0	2103.4	2436.0	2528.0	2500.0	2630.0	2748.0	2806.0	2793.0	
	2056.0	2233.0	2487.0	2598.2	2556.0	2539.0	2797.0	2788.0	2845.0	
	2146.0	2284.6	2460.0	2476.5	2441.0	2653.0	2615.0	2624.0	2521.0	
2217.0	2331.0	2632.0	2670.0	2650.0	2667.0	2740.0	2822.0	2829.6		

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Table 2 (continued)

	Sex	Baseline	8th Day	19th Day	26nd Day	37th Day	50th Day	64th Day	78th Day	89th Day	
Prophylactic Dose- Intra-Nasal (PD- IN)	♂	2033.0	2093.2	Euthanized on 15th Day							
		1763.0	1697.0								
		1986.0	2139.3								
		1947.0	2180.7	2381.0	2547.0	Euthanized on 29th Day					
		2256.0	2380.6	2540.0	2517.0						
		2007.0	2114.6	2212.0	2287.0	2292.0	2445.0	2450.0	2514.0	2519.0	
		1915.0	2007.3	2086.0	2076.0	2097.0	2143.0	2170.0	2175.0	2086.0	
		2015.0	2166.1	2301.0	2335.0	2308.0	2334.0	2616.0	2608.0	2558.2	
		2162.0	2298.8	2539.0	2577.0	2621.0	2514.0	2575.0	2578.0	2579.0	
	♀	2047.0	2203.9	2356.0	2444.0	2414.0	2461.0	2642.0	2608.0	2684.4	
		1217.4	1197.0	Euthanized on 15th Day							
		1925.7	2133.0								
		1829.7	1988.0	2082.0	2231.1	Euthanized on 29th Day					
		2051.6	2187.0	2422.0	2335.2						
		1982.1	2115.0	2257.0	2252.5						
		1923.7	2123.0	2382.0	2466.0	2489.0	2506.0	2753.0	2709.0	2681.0	
		1905.3	2117.0	2280.0	2418.3	2441.0	2339.0	2398.0	2370.0	2160.0	
		1920.1	2050.0	2278.0	2334.3	2382.0	2432.0	2580.0	2532.0	2489.0	
		2053.8	2120.0	2303.0	2198.4	1976.0	1787.0	1556.0	1335.0	-	
2126.0	2124.0	2353.0	2408.0	2395.0	2386.0	2446.0	2523.0	2535.2			

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Table 2 (continued)

	Sex	Baseline	8th Day	19th Day	26nd Day	37th Day	50th Day	64th Day	78th Day	89th Day	
Prophylactic Dose- Oral (PD-OR)	♂	1855.0	2028.5	Euthanized on 15th Day							
		1575.0	1653.0								
		2105.0	2175.4								
		1669.0	1705.5	1736.0	1701.0	Euthanized on 29th Day					
		2040.0	2207.5	2310.0	2260.0						
		2010.0	2111.3	2219.0	2300.0	2302.0	2318.0	2344.0	2466.0	2423.0	
		2080.0	2212.2	2360.0	2395.0	2358.0	2192.0	2658.0	2624.0	2640.0	
		2119.0	2240.6	2453.0	2459.0	2382.0	2402.0	2675.0	2686.0	2697.0	
		2011.0	2135.1	2317.0	2294.0	2202.0	2365.0	2595.0	2575.0	2538.0	
	♀	2223.0	2315.7	2465.0	2559.0	2437.0	2446.0	2490.0	2504.0	2540.0	
		1916.1	2122.0	Euthanized on 15th Day							
		2172.5	2315.0								
		2026.3	2163.0	2290.0	2351.8	Euthanized on 29th Day					
		2051.3	2152.0	2475.0	2556.1						
		2248.2	2357.0	2577.0	2636.1						
		1872.5	1962.0	2119.0	2182.1	2158.0	2093.0	1709.0	1802.0	1646.0	
		1240.0	1403.0	1755.0	1987.2	2127.0	2279.0	2452.0	2470.0	2197.2	
		1786.4	1862.0	2053.0	2141.3	2158.0	2290.0	2375.0	2431.0	2296.0	
		1965.3	2056.0	2244.0	2301.0	2349.0	2389.0	2512.0	2560.0	2553.7	
2329.9	2464.0	2656.0	2785.2	2697.0	2826.0	2866.0	2867.0	2845.0			

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Table 2 (continued)

	Sex	Baseline	8th Day	19th Day	26nd Day	37th Day	50th Day	64th Day	78th Day	89th Day
Average Dose (AD: 5xPD) – Intra-Nasal (AD-IN)	♂	1987.0	2174.3	Euthanized on 15th Day						
		1604.0	1498.0							
		2176.0	2506.3							
		1973.0	2087.9	2251.0	2283.0	Euthanized on 29th Day				
		2168.0	2338.5	2521.0	2532.0					
		1973.0	2190.7	2340.0	2344.0	2325.0	2331.0	2397.0	2457.0	2502.0
		1944.0	2051.3	2145.0	2254.0	2236.0	2248.0	2381.0	2328.0	2412.0
		1951.0	1999.8	2132.0	2180.0	2338.0	2213.0	2212.0	2212.0	2065.0
		2092.0	2341.8	2511.0	2508.0	2492.0	2556.0	2462.0	2491.0	2487.0
	2166.0	2297.8	2519.0	2541.0	2460.0	2532.0	2287.0	2298.0	2338.0	
	1687.4	1775.0	Euthanized on 15th Day							
	2162.3	2278.0								
	1745.2	1831.0	1986.0	2103.8	Euthanized on 29th Day					
	2088.8	2237.0	2450.0	2696.0						
	2162.0	2343.0	2464.0	2630.7						
	1561.3	1675.0	1873.0	1984.6	2325.0	2022.0	2140.0	2134.0	2252.6	
	1841.7	1982.0	2038.0	2157.3	2236.0	2218.0	2299.0	2365.0	2346.5	
	1967.0	2074.0	2260.0	2388.6	2338.0	2415.0	2497.0	2570.0	2536.4	
	1891.5	2068.0	2219.0	2325.1	2492.0	2480.0	2625.0	2657.0	2631.5	
2113.1	2163.0	2312.0	2399.4	2460.0	2675.0	2777.0	2794.0	2785.0		

Table 3.1
Day 15th - Haematological profile of rats exposed to recombinant HPV vaccine.

Group	Time Point	Sex	HGB (g/dl)	RBC (10E6/mm3)	WBC (10E3/mm3)	HCT (%)	MCV (µm3)	MCH (pg)	MCHC (g/dl)	PLT (10E3/mm3)	Neutrophils (%)	Lymphocytes (%)	Monocytes (%)	Eosinophils (%)
Vehicle Control	15th Day	♂	18.3	8.98	15.55	48.6	54.1	20.3	376	802	10	86	3	1
		♀	17.6	8.43	9.87	46.0	54.6	20.8	382	778	15	76	5	1
		♂	18.2	8.73	10.76	47.1	54.0	20.8	386	892	12	83	3	0
		♀	17.8	8.79	11.63	47.4	53.9	20.2	375	717	15	80	4	1
		♂	19.3	9.05	11.84	50.1	55.3	21.3	385	909	23	73	3	1
		♀	17.9	8.48	13.32	46.7	55.0	21.1	384	774	15	80	4	1
Experimental Control	15th Day	♂	18.2	8.82	10.07	47.5	52.9	20.4	386	776	24	72	3	1
		♀	18.3	8.98	10.07	47.5	52.9	20.4	386	776	24	72	3	1
		♂	18.1	8.77	12.01	48.2	55.0	20.7	377	943	18	78	3	1
		♀	17.6	8.43	5.55	46.3	54.9	20.9	38.1	881	45	49	4	2
		♂	17.2	8.49	13.52	45.8	54.0	20.3	376	966	12	82	5	1
		♀	18.4	9.03	10.32	48.4	53.6	20.4	38.1	1066	15	78	3	4
Prophylactic Dose	15th Day	♂	18.1	9.06	9.41	46.7	51.6	20.0	38.7	1256	14	76	8	2
		♀	17.8	8.51	13.91	46.2	54.3	20.9	38.4	960	15	82	2	1
		♂	17.8	8.30	12.34	45.7	55.0	21.4	38.9	820	14	83	2	1
		♀	18.1	8.52	9.02	47.3	55.5	21.2	38.3	889	19	76	4	1
		♂	17.0	9.02	7.49	44.8	49.7	18.9	38.0	831	25	69	4	2
		♀	17.9	8.81	9.09	46.1	52.3	20.3	38.8	972	17	76	4	3
Average Dose (Intra-Nasal)	15th Day	♂	18.7	9.28	8.80	48.2	51.9	20.1	38.8	882	18	76	4	2
		♀	15.5	7.35	10.18	41.9	57.0	21.1	37.1	869	14	81	4	1
		♂	17.6	8.37	9.78	47.0	56.1	21.1	37.5	964	12	83	4	1
		♀	18.2	9.13	13.55	48.0	52.6	20.0	38.0	836	13	82	4	1
		♂	17.8	8.33	13.67	44.2	53.1	21.3	40.2	1293	12	85	2	1
		♀	17.3	8.20	9.01	44.4	54.1	21.1	39.0	973	17	78	4	1
Average Dose (Intra-Nasal)	15th Day	♂	16.9	8.19	7.26	43.0	52.5	20.6	39.3	1078	12	84	3	1
		♀	17.9	8.74	13.74	46.1	52.7	20.4	38.7	943	14	83	2	1
		♂	17.0	8.38	8.43	45.7	56.3	20.3	37.3	678	18	79	2	1
		♀	18.0	8.68	12.48	48.9	56.3	20.7	36.8	1091	13	84	3	0
		♂	17.8	8.41	13.36	44.9	53.5	21.2	39.6	993	15	81	3	1
		♀	18.7	9.12	12.16	48.3	52.9	20.5	38.8	1003	14	79	5	2
Average			16.6	8.27	9.84	41.6	50.3	20.1	39.9	885	20	75	4	1

Table 3.2
Day 29th - Haematological profile of rats exposed to recombinant HPV vaccine.

Group	HGB (g/dl)	RBC (10E6/mm3)	WBC (mm3)	HCT (%)	MCV (µm3)	MCH (pg)	MCHC (g/dl)	PLT (10E3/mm3)	Neutrophils (%)	Lymphocytes (%)	Monocytes (%)	Eosinophils (%)
Vehicle Control	16.8	8.92	14.8	49.3	55.2	18.8	34.1	547	10	86	3	1
	15.1	8.24	11.1	43.8	53.1	18.3	34.5	662	12	85	2	1
	15.1	8.23	10.4	44.4	54.0	18.3	33.9	609	15	80	3	2
	15.7	8.47	10.7	45.1	53.3	18.6	34.9	575	24	70	4	2
Experimental Control	15.7	8.47	6.8	44.6	52.7	18.6	35.3	640	16	80	3	1
	17.8	9.47	5.0	50.6	53.5	18.8	35.2	723	18	75	5	2
	16.3	8.73	12.0	47.2	54.0	18.6	34.5	582	17	78	3	2
	14.7	8.19	7.6	43.1	52.7	18.0	34.2	555	15	80	3	2
Oral	16.1	8.83	13.7	47.2	53.5	18.2	34.0	612	11	84	4	1
	17.2	9.34	7.8	48.3	51.6	18.4	35.7	596	25	70	4	1
	17.2	9.15	8.1	48.7	53.3	18.8	35.3	608	20	75	4	1
	15.2	7.65	6.2	42.1	55.0	19.9	36.2	541	23	72	3	2
Prophylactic Dose	14.8	7.81	7.8	42.6	54.6	18.9	34.7	576	17	80	2	1
	14.8	7.93	10.9	43.1	54.5	18.7	34.3	603	15	82	2	1
	15.5	8.09	6.8	43.1	54.1	18.5	34.2	569	18	78	2	2
	15.9	8.16	8.1	44.2	54.1	19.5	36.1	520	17	77	4	2
Average Dose (Intra-Nasal)	16.8	9.14	7.8	47.4	51.8	18.4	35.5	695	18	75	5	2
	16.7	8.61	6.3	46.6	54.1	19.4	35.9	590	30	65	3	2
	15.5	8.09	6.8	44.4	54.9	19.1	34.8	591	16	80	3	1
	15.0	8.18	7.4	43.8	53.4	18.3	34.3	628	15	80	4	1
Oral	15.9	8.30	9.9	46.6	56.1	19.1	34.0	618	13	81	4	2
	15.7	8.31	10.3	44.0	53.0	18.9	35.8	569	22	73	3	2
	17.1	9.09	10.7	47.9	52.7	18.8	35.7	634	18	76	4	2
	15.4	8.22	9.4	42.6	51.8	18.8	36.2	596	19	78	2	1
Average Dose (Intra-Nasal)	15.3	8.31	8.2	44.0	52.9	18.5	34.9	602	25	70	4	1
	15.2	8.46	11.5	43.4	51.3	18.0	35.1	628	22	75	2	1
	16.2	8.90	9.8	46.9	52.7	18.1	34.4	603	26	70	3	1
	15.6	8.06	6.4	43.0	53.3	19.3	36.3	574	20	76	2	2
Average Dose (Intra-Nasal)	15.4	7.94	7.1	42.4	53.4	19.3	36.2	630	26	70	3	1
	15.1	7.85	8.8	41.1	52.4	19.3	36.8	464	25	70	3	2
	15.9	8.20	7.8	46.0	56.0	19.4	34.6	598	20	75	3	2
	15.3	8.31	11.0	43.6	52.5	18.4	35.1	592	30	65	4	1
Average Dose (Intra-Nasal)	16.3	9.06	6.1	47.2	52.0	18.0	34.6	624	25	70	3	2
	15.6	8.31	9.7	43.6	52.4	18.8	35.9	585	20	73	5	2
	16.3	8.66	9.5	45.0	52.0	18.8	35.9	596	22	75	2	1
	15.7	8.18	8.3	43.8	53.5	19.2	35.8	460	19	78	2	1

Table 3.3
Day 93rd - Haematological profile of rats exposed to recombinant HPV vaccine.

Group	Time Point	Sex	HGB (g/dl)	RBC (10E6/mm ³)	WBC (10E3/mm ³)	HCT (%)	MCV (μm ³)	MCH (pg)	MCHC (g/dl)	PLT (10E3/mm ³)	Neutrophils (%)	Lymphocytes (%)	Mono-cytes (%)	Eosino-phils (%)	
Vehicle Control	93rd Day	♂	17.7	9.06	9.50	49.4	54.5	19.6	35.9	781	22	72	5	1	
			16.8	9.23	10.66	46.5	50.4	18.2	36.1	1039	30	65	4	1	
			17.8	9.14	8.41	48.2	52.7	19.4	36.9	956	28	68	3	1	
		18.4	9.53	8.86	50.0	52.5	19.3	36.7	1024	24	72	3	1		
		20.1	10.30	9.35	52.7	51.1	19.5	38.1	762	26	70	3	1		
		18.7	9.35	12.71	48.2	51.6	20.0	38.7	749	23	73	3	1		
		17.6	9.01	10.19	48.3	53.6	19.5	36.4	1104	15	82	2	1		
		17.0	8.52	6.50	46.8	54.9	20.0	36.4	1002	17	80	2	1		
		17.3	8.70	2.75	47.4	54.5	19.8	36.4	878	32	64	3	1		
	18.5	9.38	10.18	48.8	52.0	19.7	37.8	945	20	77	2	1			
	17.3	8.41	12.41	45.2	53.8	20.5	38.2	1021	24	72	3	1			
	17.7	9.10	6.67	46.9	51.6	19.5	37.7	1133	20	74	5	1			
	Experimental Control	Intra-Nasal 93rd Day	♂	19.2	10.03	9.39	51.5	51.3	19.1	37.2	959	18	76	5	1
				18.0	9.48	8.20	48.8	51.4	19.0	37.0	1299	18	73	8	1
				17.9	9.06	7.63	48.8	53.9	19.8	36.7	1185	22	75	2	1
			18.3	9.71	12.06	49.9	59.4	18.8	36.6	1145	20	75	4	1	
			17.1	8.68	11.55	43.2	49.8	19.7	39.5	1034	25	71	3	1	
			19.0	9.73	9.36	49.9	51.3	19.6	38.1	823	30	65	3	2	
17.1			8.52	7.96	46.2	54.2	20.1	37.0	852	34	60	4	2		
18.2			9.46	8.87	49.6	52.4	19.2	36.7	981	29	65	4	2		
18.0			8.94	7.34	48.1	53.8	20.1	37.4	1060	17	80	2	1		
18.3		9.02	10.40	47.9	53.1	20.3	38.1	859	20	76	3	1			
18.4		9.03	8.17	47.5	52.6	20.3	38.7	840	19	76	4	1			
Oral 93rd Day		♂	18.2	9.26	12.59	48.4	52.3	19.6	37.5	1144	28	67	4	1	
			16.9	8.88	6.84	45.8	51.6	19.1	37.0	1056	35	58	5	2	
			17.5	9.11	15.37	48.1	52.8	19.2	36.5	951	25	70	4	1	
		19.0	9.78	9.68	48.7	49.8	19.4	39.0	802	35	61	3	1		
		18.2	9.45	9.28	47.7	50.5	19.3	38.2	885	26	69	3	2		
		16.8	8.30	7.74	44.2	53.3	20.2	37.9	1206	18	78	3	1		
		17.2	8.70	9.79	45.8	52.7	19.7	37.5	1106	18	76	5	1		
	16.9	8.40	7.13	43.8	52.2	20.2	38.6	1104	22	75	2	1			
	17.0	8.62	9.57	46.2	53.7	19.7	36.7	1110	20	77	2	1			
17.2	8.61	9.56	47.7	55.3	20.0	36.2	964	15	82	2	1				
17.7	8.81	11.80	47.6	54.1	20.1	37.2	887	19	77	3	1				

(continued on next page)

Table 3.3 (continued)

Group	Prophylactic	Intra-Nasal	Time Point	Sex	HGB (g/dl)	RBC (10E6/mm3)	WBC (10E3/mm3)	HCT (%)	MCV (µm3)	MCH (pg)	MCHC (g/dl)	PLT (10E3/mm3)	Neutrophils (%)	Lymphocytes (%)	Mono-cytes (%)	Eosinophils (%)		
Prophylactic Dose	93rd Day	♂	18.6	7.30	7.73	51.1	49.6	18.1	36.5	864	27	68	3	2				
			16.9	8.59	11.45	45.5	53.0	19.7	883	25	68	5	68	5	2			
			16.4	8.92	7.39	44.3	49.6	19.4	874	35	58	5	58	5	2			
			17.7	9.15	9.27	45.6	49.8	19.3	1032	26	69	4	69	4	1			
			17.0	8.83	7.84	44.1	50.0	19.3	38.8	1061	20	76	3	1				
	93rd Day	♀	16.8	8.67	9.62	43.4	50.0	19.4	38.7	875	29	67	3	1				
			17.2	8.63	6.90	45.0	52.1	20.0	38.3	903	22	72	5	1				
			17.3	8.68	5.34	46.4	53.4	19.9	37.2	947	32	65	2	1				
			17.4	8.69	7.27	47.2	54.3	20.0	36.8	902	35	61	3	1				
			16.9	8.91	7.19	45.7	51.3	19.0	36.9	794	27	63	3	2				
Average Dose (Intra-Nasal)	93rd Day	♂	17.7	9.45	11.16	48.9	51.8	18.8	36.3	758	29	64	5	2				
			18.0	9.17	5.03	46.2	50.3	19.7	802	28	65	5	2					
			17.1	8.95	9.05	44.4	49.6	19.2	38.6	786	26	68	4	2				
			16.9	8.57	8.66	48.2	56.3	19.7	35.1	222	25	69	4	2				
			16.3	8.84	5.32	43.0	48.6	18.4	37.9	791	35	57	6	2				
	93rd Day	♀	17.4	8.70	6.37	46.8	53.8	20.1	37.3	897	26	70	3	1				
			17.4	8.76	7.40	47.3	54.0	19.9	36.8	847	27	68	3	2				
			18.0	8.97	8.15	48.3	53.8	20.0	37.2	799	26	70	3	2				
			16.8	8.46	4.92	44.2	52.3	19.8	37.9	920	28	68	2	2				
			16.8	8.62	6.51	43.9	50.9	19.5	38.2	976	20	75	4	1				
Average Dose (Intra-Nasal)	93rd Day	♂	16.6	8.10	8.93	40.9	50.5	20.5	40.7	1271	28	68	3	1				
			19.9	10.33	8.86	54.5	52.8	19.3	36.6	792	27	65	6	2				
			18.7	9.34	11.38	49.1	52.5	20.0	38.2	956	21	73	6	0				
			17.2	9.22	7.78	45.4	49.2	18.7	37.9	977	22	72	5	1				
			17.3	9.40	9.94	45.6	48.5	18.4	38.0	940	20	72	6	2				
Average Dose (Intra-Nasal)	93rd Day	♀	17.5	9.08	10.88	46.4	51.1	19.2	37.7	864	20	73	5	2				
			18.0	9.38	8.52	47.4	50.5	19.2	37.9	922	21	73	5	1				
			13.3	6.58	10.89	35.6	54.0	20.3	37.5	1445	20	74	5	1				
			17.2	8.75	11.99	44.8	51.2	19.6	38.3	848	25	69	5	1				
			15.9	8.00	9.83	40.0	50.0	19.9	39.7	848	25	69	5	1				
Average Dose (Intra-Nasal)	93rd Day	♀	17.3	8.64	13.53	46.4	53.8	20.1	37.4	819	23	75	4	0				
			18.0	9.21	7.33	49.0	53.2	19.5	36.7	843	25	71	2	2				
			17.3	3.57	13.97	47.4	55.3	20.2	36.6	942	18	79	2	2				

Table 4.1
Day 15th - Haematological profile of rabbits exposed to recombinant HPV vaccine.

Group	Time Point	Sex	HGB (g/dl)	RBC (10E6/mm ³)	WBC (10E3/mm ³)	HCT (%)	MCV (µm ³)	MCH (pg)	MCHC (g/dl)	PLT (10E3/mm ³)	Neutrophils (%)	Lymphocytes (%)	Mono-cytes (%)	Eosino-philis (%)	Baso-philis (%)
Vehicle Control	15th Day	♂	12.9	6.15	6.45	38.4	62.5	20.9	33.5	727	15	78	4	1	2
		♀	15.0	6.89	11.07	44.2	64.2	21.8	34.0	251	20	73	3	2	2
Experimental Control	15th Day	♀	16.3	7.34	14.65	44.4	60.5	22.2	36.7	627	35	55	5	2	3
		♂	12.9	6.15	12.28	36.6	59.5	21.0	35.3	1050	48	46	4	0	2
		♀	14.5	6.28	10.84	38.0	60.5	23.1	38.1	782	25	70	2	1	2
	IN	♂	13.4	5.84	10.13	38.5	65.9	23.0	34.8	1179	45	49	4	1	1
		♀	14.6	5.81	10.68	37.7	64.9	25.1	38.6	1566	24	69	3	1	3
		♂	12.3	5.13	11.48	31.3	61.1	24.0	39.2	972	30	65	4	0	1
Oral	15th Day	♂	15.9	7.22	4.84	43.7	60.6	22.0	36.3	627	30	62	4	2	2
		♀	17.0	7.45	8.09	46.9	62.9	22.8	36.2	615	20	74	4	1	1
		♂	13.9	6.18	8.88	36.7	59.3	22.5	37.9	1789	22	70	4	1	3
	IN	♂	14.2	6.19	8.08	38.9	62.8	23.0	36.6	698	22	71	3	1	3
		♀	14.2	6.07	9.77	40.1	66.1	23.4	35.4	752	27	66	5	1	1
		♂	13.7	6.14	7.07	40.1	65.4	22.2	34.0	1619	62	32	2	1	1
Prophylactic Dose (PD)	15th Day	♂	15.9	7.24	10.38	45.7	63.1	21.9	34.8	824	20	75	2	1	2
		♀	16.6	8.07	5.18	45.2	56.0	20.6	36.8	344	37	55	5	1	2
		♂	13.7	5.75	8.53	37.0	64.3	23.8	37.0	998	25	70	2	1	2
	Oral	♂	14.5	6.26	10.81	42.3	67.5	23.2	34.4	682	30	64	3	1	2
		♀	15.4	6.35	8.46	40.9	64.5	24.2	37.5	657	20	75	3	1	1
		♂	16.0	7.46	9.31	44.2	59.3	21.4	36.1	480	22	70	4	2	2
Average Dose (IN)	15th Day	♀	14.0	6.09	10.86	37.7	61.9	22.9	37.0	712	18	75	5	1	1
		♂	14.7	6.13	6.07	39.6	64.7	23.9	37.0	642	18	76	2	1	3
		♂	15.9	7.04	8.77	45.6	64.7	22.6	34.9	563	30	64	3	1	2
	Average Dose (IN)	♀	12.8	5.96	4.71	36.3	60.9	21.5	35.2	1811	55	40	3	1	1
		♂	14.4	6.34	9.72	37.0	58.4	22.8	39.0	540	25	69	2	1	3
		♀	14.4	6.16	12.64	39.8	64.6	23.4	36.2	594	35	57	5	1	2
♀	13.3	5.94	8.27	36.1	60.8	22.4	36.9	925	25	70	2	1	2		

Table 4.2
Day 29th - Haematological profile of rabbits exposed to recombinant HPV vaccine.

Group	Time Point	Sex	HGB (g/dl)	RBC (10E6/mm3)	WBC (10E3/mm3)	HCT (%)	MCV (µm3)	MCH (pg)	MCHC (g/dl)	PLT (10E3/mm3)	Neutrophils (%)	Lymphocytes (%)	Mono-cytes (%)	Eosino-phils (%)	Baso-phils (%)
Vehicle Control	29th Day	♂	15.9	7.58	12.93	44.1	58.2	20.9	36.0	1071	30	62	5	2	1
			15.0	6.12	8.95	40.2	65.7	24.5	37.3	546	35	58	3	2	2
		♀	14.6	6.28	8.27	39.4	62.8	23.3	37.1	511	23	70	4	1	2
			15.1	6.41	9.35	40.5	63.2	23.6	37.4	629	24	70	3	1	2
Experimental Control	IN	♂	15.4	6.36	12.70	40.6	63.8	24.2	37.9	539	15	78	4	1	2
			15.3	6.87	9.16	42.3	61.6	22.2	36.0	355	18	75	4	2	1
		♀	17.0	7.43	9.19	46.7	62.8	22.9	36.5	508	25	69	3	1	2
			14.2	6.25	12.72	37.1	59.3	22.7	38.2	568	15	79	3	1	2
			13.1	5.69	18.80	36.2	63.6	23.0	36.2	925	50	41	6	1	2
	Oral	♂	14.3	6.32	5.22	37.2	58.8	22.6	38.4	276	19	75	3	1	2
			14.9	7.26	13.36	40.4	55.7	20.5	36.9	739	30	62	6	1	1
		♀	15.1	6.87	11.30	41.8	60.8	21.9	36.1	648	35	57	6	0	2
			16.2	6.84	7.22	43.3	63.3	23.7	37.4	468	25	70	2	1	2
			13.1	5.08	9.47	34.5	67.8	25.8	38.1	662	25	69	4	0	2
ProphylactidN Dose (PD)	Oral	♂	16.3	7.07	8.52	44.8	63.3	23.1	36.4	699	25	70	2	1	2
			14.4	6.38	12.47	39.1	61.3	22.6	36.9	721	35	58	4	1	2
		♀	16.5	7.04	8.71	45.9	65.2	23.5	36.1	806	37	55	5	2	1
			16.3	6.59	10.59	44.1	66.9	24.7	36.9	744	20	75	2	1	2
			13.4	5.97	17.55	34.8	58.4	22.4	38.4	747	26	68	3	1	2
	IN	♂	15.4	6.61	6.95	40.4	61.2	23.2	38.0	662	13	80	4	1	2
			15.1	6.77	15.96	41.0	60.5	22.3	36.9	1054	58	38	2	0	2
		♀	15.0	6.67	12.07	40.2	60.3	22.4	37.3	941	38	56	4	1	1
			15.6	6.68	10.49	42.2	63.1	23.4	37.0	524	25	69	4	1	1
			17.0	6.66	7.50	45.1	67.8	25.6	37.8	544	12	82	3	1	2
Average Dose (IN)	♂	13.6	5.76	10.99	34.5	59.9	23.5	39.3	713	35	57	5	1	2	
		16.1	6.65	11.04	44.6	67.1	24.1	36.0	876	30	64	4	1	1	
	♀	15.1	6.18	8.22	39.8	64.4	24.4	38.0	657	40	53	5	1	1	
		14.9	6.27	10.73	39.0	62.2	23.7	38.2	412	20	72	4	2	2	
		13.8	5.76	8.74	37.0	64.2	23.9	37.3	359	19	74	4	1	2	
			14.5	5.76	11.64	36.8	63.8	25.1	39.3	672	22	70	3	1	4

Table 4.3
Day 93rd - Haematological profile of rabbits exposed to recombinant HPV vaccine.

Group	Time Point	Sex	HGB (g/dl)	RBC (10E6/mm3)	WBC (10E3/mm3)	HCT (%)	MCV (µm3)	MCH (pg)	MCHC (g/dl)	PLT (10E3/mm3)	Neutrophils (%)	Lymphocytes (%)	Mono-cytes (%)	Eosino-phils (%)	Baso-phils (%)		
Vehicle Control	93rd Day	♂	14.5	6.40	16.31	41.5	64.8	22.6	34.9	679	35	60	2	1	2		
			15.6	7.27	9.15	46.0	63.3	21.4	33.9	690	32	62	2	2	2		
			16.8	3.35	12.11	22.5	67.2	20.2	30.0	2000	40	52	5	1	2		
			14.4	6.79	10.65	40.5	59.7	21.3	35.6	526	65	30	2	1	2		
			15.5	6.89	9.03	44.9	65.2	22.5	34.6	512	20	75	2	1	2		
		♀	13.2	6.10	8.67	38.4	63.0	21.7	34.4	691	38	55	3	2	2		
			13.9	6.26	8.63	42.0	67.1	22.2	33.1	212	25	69	2	1	3		
			14.9	6.43	9.64	42.1	65.5	23.2	35.5	571	25	66	5	1	3		
			13.6	6.04	6.89	40.5	67.1	22.4	33.5	572	20	75	2	1	2		
			16.9	7.59	9.79	48.9	64.3	22.3	34.6	539	22	70	3	2	3		
		Experimental Control	93rd Day	♂	14.8	6.78	6.99	41.5	61.2	21.9	35.7	480	22	72	2	1	3
					15.7	6.92	12.71	45.4	65.6	22.7	34.5	408	60	35	2	1	2
					15.3	6.58	7.80	44.5	67.6	23.3	34.4	446	30	65	3	1	1
					12.4	5.26	20.21	35.2	66.9	23.6	35.2	877	49	44	5	0	2
					13.4	6.32	8.17	39.7	62.7	21.2	33.7	715	40	55	2	1	2
♀	11.0			4.85	10.53	33.8	69.8	22.6	32.4	1288	55	39	3	1	2		
	14.3			6.23	7.73	40.9	65.6	22.9	35.0	372	35	57	2	2	4		
	13.1			5.96	8.91	37.7	63.2	22.0	34.7	514	22	70	4	1	3		
	14.9			7.16	7.45	42.0	58.6	20.9	35.6	464	35	58	2	2	3		
	14.1			6.47	10.21	41.7	64.4	21.8	33.9	541	17	78	1	1	3		
Oral	93rd Day			♂	10.5	5.06	8.81	33.6	66.5	20.7	31.1	1432	40	50	6	2	2
					12.1	5.89	8.40	36.8	62.4	20.6	33.0	1506	45	48	5	1	1
					15.0	6.86	8.64	45.5	66.3	21.8	32.9	457	16	80	1	1	2
					16.7	7.34	11.36	52.0	70.8	22.7	32.0	177	15	80	2	1	2
					15.7	7.00	6.59	46.0	65.7	22.5	34.2	417	28	66	2	1	3
		♀	13.2	6.02		38.0	63.2	21.9	34.7	826	70	22	4	1	3		
					26.49												
			13.4	6.02	8.54	39.6	65.8	22.3	33.8	372	20	73	2	1	4		
			14.1	6.37	13.33	39.2	61.5	22.2	36.0	479	18	74	2	1	5		
			13.3	6.02	10.39	38.6	64.1	22.1	34.5	756	20	74	2	2	2		
13.6	5.99	6.04	39.5	65.9	22.7	34.5	392	28	65	2	2	3					

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Table 4.3 (continued)

Group	Time Point	Sex	HGB (g/dl)	RBC (10E6/mm3)	WBC (10E3/mm3)	HCT (%)	MCV (um3)	MCH (pg)	MCHC (g/dl)	PLT (10E3/mm3)	Neutro- phils (%)	Lymph- ocytes (%)	Mono- cytes (%)	Eosino- phils (%)	Baso- phils (%)	
Prophylactic Dose (PD)	93rd Day	♂	15.1	6.61	11.73	40.9	61.8	22.8	36.9	446	30	63	4	1	2	
			13.6	6.45	5.71	41.5	64.3	21.1	32.9	1061	40	52	5	2	1	
			14.1	6.68	8.21	40.9	61.2	21.1	34.5	620	30	63	3	2	2	
		15.2	6.83	6.93	45.4	66.4	22.3	33.6	457	18	78	2	1	1		
		12.6	6.06	7.01	34.8	57.4	20.8	36.2	681	30	64	2	2	1	3	
		15.3	6.65	21.58	44.4	66.8	22.9	34.3	825	50	41	5	1	3	3	
	93rd Day	♀	12.4	6.22	3.88	37.2	59.9	20.0	33.4	661	43	47	6	2	2	4
			14.8	6.81	7.02	42.4	62.3	21.7	34.9	462	20	72	2	2	2	4
			12.3	5.46	9.92	34.4	63.0	22.5	35.7	598	40	54	3	1	2	2
		13.7	6.27	7.52	40.2	64.1	21.8	34.0	602	25	68	2	3	2	2	
		12.8	5.70	13.25	38.6	67.8	22.5	33.2	1099	50	44	3	1	2	2	
		14.5	6.51	9.45	40.7	62.5	22.4	35.7	476	20	75	2	2	2	2	
Oral	93rd Day	♂	14.6	6.74	8.57	42.1	62.5	21.7	34.7	638	31	65	2	1	1	
			16.1	7.44	6.69	45.3	61.0	21.7	35.5	554	22	72	2	2	2	
			11.7	5.82	12.08	34.9	60.0	20.2	33.6	909	50	43	5	1	1	
		9.3	4.78	17.45	28.4	59.3	19.5	32.8	1206	48	45	5	1	1		
		14.5	6.24	10.05	40.5	64.9	23.2	35.8	561	25	69	2	1	3		
		13.5	5.95	7.74	38.1	64.1	22.7	35.4	374	26	67	2	2	3		
	Average Dose (IN)	93rd Day	♂	13.4	5.77	7.44	38.1	66.1	23.2	35.1	694	20	74	1	1	4
				14.7	6.43	8.51	41.2	64.0	22.8	35.6	371	20	69	4	2	5
				15.0	6.74	11.33	42.7	63.3	22.2	35.1	598	35	60	2	2	2
		12.0	5.53	11.20	35.5	64.2	21.7	33.7	1532	48	43	5	2	2		
		13.3	6.04	9.35	38.3	63.4	22.0	34.6	902	36	55	5	1	3		
		13.3	6.13	9.58	37.5	61.2	21.6	35.4	584	36	59	2	1	2		
Average Dose (IN)	93rd Day	♀	16.4	7.90	11.67	50.6	64.1	20.7	32.4	727	38	52	4	3	3	
			13.8	5.89	7.02	38.5	65.3	23.4	35.8	504	28	65	3	1	3	
			14.7	6.57	8.52	42.7	65.0	22.4	34.5	608	18	74	2	2	4	
	13.3	6.08	8.92	39.7	65.3	22.0	33.6	789	29	65	2	2	2			
	14.2	6.24	8.71	42.5	68.1	22.7	33.4	421	20	72	2	2	2			
	14.2	6.24	8.71	42.5	68.1	22.7	33.4	421	20	72	2	2	2			

Table 5
Biochemical profile of rats administered with rSt.HPV.

Group	Euthanization Day	Sex	ALT (U/L)	AST (U/L)	ALP (U/L)	Creatinine (mg/dL)	Total Bilirubin (mg/dL)	Urea (mg/dL)	Glucose (mg/dL)	Calcium (mg/dL)	Total Protein (g/dL)	Albumin (g/dL)
Vehicle Control	15th Day	♂	48	99	366	0.9	0.1	40.0	90.0	10.5	5.9	3.9
			45	99	309	0.9	0.1	43.0	107.0	10.2	5.5	3.8
			42	93	360	0.8	0.1	41.0	74.0	10.9	5.6	3.8
	29th Day	♀	42	120	195	0.9	0.2	38.0	85.0	10.6	5.7	3.6
			42	108	231	0.9	0.3	51.0	89.0	10.7	5.8	3.8
			42	108	252	0.8	0.2	41.0	67.0	11.2	6.1	3.9
		♂	60	138	342	0.8	0.2	26.0	96.0	12.0	7.1	4.2
			42	111	303	0.8	0.1	32.0	103.0	13.4	6.6	4.0
			45	102	321	0.7	0.2	22.0	88.0	12.0	7.0	3.9
	93rd Day	♀	51	105	249	0.8	0.2	29.0	110.0	11.7	7.0	4.1
			51	114	219	0.8	0.1	25.0	93.0	11.8	6.7	4.3
			42	84	186	0.6	0.2	43.0	79.0	12.7	7.5	4.2
		♂	87	144	270	0.8	0.2	29	95	9.7	6.7	3.4
			84	141	276	1.0	0.2	32	127	9.9	6.6	3.2
			66	126	228	1.1	0.2	35	89	10.2	7.3	3.5
			81	135	333	0.7	0.2	37.0	115.0	10.8	7.4	3.7
			60	162	201	0.9	0.3	33.0	145.0	10.9	6.9	3.7
			87	222	135	1.2	0.6	42	106	10.0	6.6	3.3
	♀	81	162	159	1.1	0.2	30	75	10.3	6.7	3.5	
		72	132	213	1.1	0.2	37	88	10.1	7.2	3.8	
		54	183	120	0.9	0.3	36.0	117.0	12.0	7.3	3.9	
36		117	126	0.8	0.2	45.0	109.0	11.7	6.9	3.8		
27		102	108	0.8	0.2	34.0	104.0	11.8	7.9	4.2		

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Table 5 (continued)

Group	Euthanization Day	Sex	ALT (U/L)	AST (U/L)	ALP (U/L)	Creatinine (mg/dL)	Total Bilirubin (mg/dL)	Urea (mg/dL)	Glucose (mg/dL)	Calcium (mg/dL)	Total Protein (g/dL)	Albumin (g/dL)		
Experimental Control Intranasal (EC-IN)	15th Day	♂	54	108	327	0.8	0.1	42.0	95.0	11.3	5.4	3.6		
			60	108	294	0.8	0.1	51.0	112.0	10.8	6.4	4.2		
			33	60	246	0.8	0.2	42.0	87.0	11.1	5.6	3.5		
		♀	51	111	282	0.9	0.2	41.0	76.0	10.8	5.8	3.7		
			27	117	192	0.7	0.2	44.0	67.0	10.4	6.0	3.9		
	29th Day	♂	57	129	231	0.6	0.1	39.0	77.0	10.2	5.8	3.6		
			45	99	279	0.6	0.2	28.0	92.0	11.9	6.6	4.1		
			60	105	327	0.5	0.2	20.0	77.0	12.0	6.4	3.8		
			57	126	270	1.0	0.3	26.0	107.0	11.4	6.5	4.1		
			36	96	186	0.8	0.2	34.0	94.0	12.2	7.5	4.2		
		♀	39	105	180	0.7	0.2	47.0	84.0	11.9	7.1	4.2		
			42	105	180	0.7	0.1	29.0	89.0	12.1	6.3	4.1		
			93rd Day	♂	75	114	222	1.3	0.2	34	113	10.5	7.6	3.5
					93	153	276	1.1	0.2	32	121	9.3	6.8	3.6
					90	159	228	1.2	0.2	31	87	10.8	7.3	3.7
	75	132			213	1.0	0.2	30	88	10.7	7.6	3.5		
	75	171			174	1.0	0.2	41	80	11.4	7.5	3.5		
	♀	120	177	234	0.9	0.3	32	88	10.2	7.2	3.3			
		60	153	204	1.1	0.2	36	87	11.1	7.1	3.7			
		108	255	210	1.0	0.2	39	92	10.3	7.5	3.9			
60		132	144	0.9	0.2	27	60	10.6	6.9	3.8				
52		132	165	0.9	0.3	32.0	106.0	11.2	7.3	4.1				
45		111	129	0.7	0.3	40.0	93.0	11.8	7.9	4.4				

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Table 5 (continued)

Group	Euthanization Day	Sex	ALT (U/L)	AST (U/L)	ALP (U/L)	Creatinine (mg/dL)	Total Bilirubin (mg/dL)	Urea (mg/dL)	Glucose (mg/dL)	Calcium (mg/dL)	Total Protein (g/dL)	Albumin (g/dL)
Experimental Control Oral (EC-OR)	15th Day	♂	57	99	318	0.7	0.1	44.0	94.0	10.7	5.9	3.9
			63	111	312	0.7	0.1	58.0	124.0	10.7	6.0	3.9
			48	108	382	0.8	0.1	41.0	67.0	10.0	5.7	3.7
		♀	36	87	198	0.8	0.1	43.0	55.0	11.0	5.8	3.8
			36	96	219	0.9	0.1	52.0	77.0	11.2	5.8	3.8
			39	111	213	0.8	0.1	40.0	70.0	10.5	6.0	3.9
	29th Day	♂	57	84	300	0.7	0.3	29.0	88.0	11.9	6.4	4.1
			33	84	258	0.6	0.3	23.0	84.0	12.1	6.6	4.0
			51	84	222	0.6	0.2	25.0	96.0	11.9	6.4	4.1
		♀	42	129	180	0.7	0.2	40.0	104.0	11.8	5.9	3.9
			39	102	159	0.8	0.2	39	91	11.7	7.1	4.3
			39	99	165	0.5	0.2	29	102	11.8	6.9	4.4
	93rd Day	♂	78	132	162	1.0	0.1	35	84	9.1	6.7	3.1
			72	156	162	1.0	0.2	33	104	9.9	6.5	3.3
			57	147	156	0.7	0.2	37.0	114.0	11.0	7.4	3.8
			54	129	198	0.9	0.2	36.0	92.0	11.7	7.8	4.1
			42	120	183	0.8	0.2	37.0	106.0	11.0	7.6	3.9
			63	138	123	0.8	0.2	36.0	95.0	11.2	7.2	3.7
		♀	66	150	186	1.2	0.2	38	81	9.3	6.4	3.6
			72	156	144	1.2	0.2	40	81	9.9	6.9	3.5
			66	183	147	1.2	0.3	40	65	10.1	6.6	3.5
30			93	135	0.8	0.3	31.0	98.0	11.7	7.2	4.2	
39			120	147	0.7	0.2	34.0	82.0	11.8	7.3	4.2	
69			186	126	0.7	0.2	51.0	85.0	11.7	7.6	4.5	

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Table 5 (continued)

Group	Euthanization Day	Sex	ALT (U/L)	AST (U/L)	ALP (U/L)	Creatinine (mg/dL)	Total Bilirubin (mg/dL)	Urea (mg/dL)	Glucose (mg/dL)	Calcium (mg/dL)	Total Protein (g/dL)	Albumin (g/dL)
Prophylactic Dose Intra-Nasal (PD-IN)	15th Day	♂	51	114	288	0.6	0.1	28.0	75.0	10.2	5.5	3.8
			54	105	285	0.6	0.2	33.0	77.0	10.6	5.7	3.7
			57	90	303	0.7	0.2	43.0	83.0	11.0	6.0	3.7
	29 ^h Day	♀	33	96	270	0.7	0.2	37.0	60.0	10.6	5.4	3.4
			51	117	219	0.7	0.2	43.0	77.0	10.8	5.5	3.8
			25	96	180	0.8	0.1	35.0	76.0	10.8	5.9	3.9
		♂	66	114	285	0.7	0.3	19.0	72.0	12.0	6.3	4.0
			45	90	222	0.6	0.2	25.0	81.0	11.8	6.6	4.0
			54	105	195	0.7	0.3	34.0	73.0	12.0	6.3	4.1
	93rd Day	♀	36	84	216	0.7	0.3	32	97	12.2	6.5	4.2
			48	138	174	0.7	0.3	36	107	12.2	6.9	4.3
			51	108	174	0.8	0.2	34	80	12.4	6.9	3.9
		♂	90	144	210	0.9	0.2	34	106	11.0	7.6	3.7
			87	153	186	0.8	0.2	34	89	10.4	7.3	3.5
			78	132	168	0.7	0.3	33	94	10.4	6.7	3.6
			75	114	195	0.8	0.2	34	73	9.2	6.2	3.2
			39	117	204	0.7	0.2	34.0	82.0	11.1	6.9	3.4
			81	258	201	0.7	0.3	34.0	90.0	10.7	6.9	3.8
	♀	66	150	156	1.2	0.2	32	66	10.5	6.5	3.7	
		51	138	204	1.1	0.2	44	69	10.1	6.9	4.1	
		66	123	162	0.9	0.2	38	80	9.4	6.4	3.8	
84		195	141	0.9	0.2	21	72	10.1	6.9	3.5		

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Table 5 (continued)

Group	Euthanization Day	Sex	ALT (U/L)	AST (U/L)	ALP (U/L)	Creatinine (mg/dL)	Total Bilirubin (mg/dL)	Urea (mg/dL)	Glucose (mg/dL)	Calcium (mg/dL)	Total Protein (g/dL)	Albumin (g/dL)
Prophylactic Dose Oral (PD-OR)	15th Day	♂	39	138	354	0.6	0.2	27.0	70.0	10.6	5.5	3.7
			54	108	255	0.7	0.2	34.0	60.0	10.7	5.4	3.7
			51	96	240	0.7	0.1	42.0	73.0	10.4	6.1	3.6
		♀	69	204	204	0.8	0.1	42.0	87.0	10.7	5.9	3.9
			36	108	204	0.9	0.2	38.0	93.0	10.4	5.9	3.8
			30	72	213	0.7	0.2	30.0	77.0	10.2	5.3	3.6
	29th Day	♂	54	102	276	0.7	0.3	26.0	85.0	11.9	6.6	4.1
			60	111	279	0.6	0.2	20.0	99.0	12.4	6.3	4.1
			60	117	306	0.7	0.3	28.0	82.0	12.1	6.6	4.0
		♀	48	96	192	0.6	0.2	34	104	12.4	6.5	4.1
			54	84	216	0.7	0.1	38	100	11.9	6.5	4.1
			45	99	180	0.7	0.2	41	95	12.2	6.5	3.7
	93rd Day	♂	156	189	252	1.1	0.3	34	71	11.1	7.4	3.5
			51	159	195	0.6	0.2	35.0	86.0	11.2	5.9	3.7
			66	144	180	0.8	0.2	32.0	74.0	12.0	7.5	3.9
			45	111	201	0.7	0.2	34.0	76.0	11.5	6.9	3.8
			60	174	261	0.8	0.2	41.0	107.0	11.8	7.1	3.9
			48	123	177	0.7	0.1	41.0	88.0	10.8	6.6	3.7
		♀	54	138	141	1.0	0.2	37	76	10.1	6.1	3.5
			96	204	132	1.1	0.2	37	93	10.0	6.3	3.5
			36	105	150	0.6	0.2	48.0	64.0	11.8	7.3	4.3
45			93	156	0.7	0.1	38.0	83.0	10.9	7.1	3.8	
39			129	108	0.8	0.2	39.0	80.0	12.0	7.6	4.3	
39			123	192	0.8	0.2	43.0	55.0	12.1	7.0	3.8	

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Table 5 (continued)

Group	Euthanization Day	Sex	ALT (U/L)	AST (U/L)	ALP (U/L)	Creatinine (mg/dL)	Total Bilirubin (mg/dL)	Urea (mg/dL)	Glucose (mg/dL)	Calcium (mg/dL)	Total Protein (g/dL)	Albumin (g/dL)
Average Dose Intra-Nasal (AD-IN)	15th Day	♂	66	114	300	0.6	0.2	32.0	71.0	10.7	5.8	3.6
			54	114	345	0.6	0.1	31.0	75.0	10.4	5.3	3.5
			57	111	273	0.8	0.2	26.0	60.0	11.1	5.8	3.7
		♀	39	99	216	0.7	0.2	41.0	81.0	10.4	5.7	3.6
			30	105	201	0.8	0.2	36.0	89.0	11.1	6.1	3.9
			54	144	181	0.7	0.2	38.0	102.0	10.4	5.4	3.4
	29th Day	♂	48	105	258	0.6	0.2	24.0	77.0	11.7	6.7	4.0
			51	84	219	0.5	0.2	33.0	94.0	12.0	6.3	4.1
			39	99	231	0.8	0.2	43.0	73.0	12.4	6.8	4.4
		♀	45	105	210	0.7	0.2	46	91	12.2	6.4	3.8
			48	108	183	0.9	0.3	53	74	12.6	6.9	3.9
			42	123	219	0.8	0.3	47	71	13.2	6.6	3.9
	93rd Day	♂	150	162	234	1.0	0.3	37	86	9.4	7.5	3.3
			45	129	156	0.8	0.3	31.0	117.0	10.8	7.3	3.9
			84	240	207	0.7	0.3	46.0	87.0	11.4	7.2	3.7
			87	135	165	0.7	0.1	40.0	69.0	11.4	7.1	3.8
			90	246	201	0.7	0.2	42.0	72.0	11.3	7.1	3.8
			69	168	207	0.6	0.2	34.0	84.0	11.4	6.7	3.9
		♀	66	120	189	1.1	0.2	33	88	10.4	7.0	3.1
			54	132	162	1.0	0.5	40	85	9.6	6.7	3.8
			81	177	150	1.2	0.3	36	126	10.1	6.7	3.4
			111	198	135	0.7	0.1	46.0	89.0	11.8	6.7	3.8
			39	105	165	0.7	0.2	33.0	81.0	11.8	7.4	3.9
			36	99	156	0.6	0.2	33.0	98.0	11.1	7.1	4.1

Table 6
Biochemical profile of rabbits used for subchronic testing of rSt.HPV expressing HPV 16 and 18 L1 proteins.

Group	Euthanization Day	Sex	ALT (U/L)	AST (U/L)	ALP (U/L)	Creatinine (mg/dL)	Total Bilirubin (mg/dL)	Urea (mg/dL)	Glucose (mg/dL)	Calcium (mg/dL)	Total Protein (g/dL)	Albumin (g/dL)
Vehicle Control	14th Day	♂	36.00	21.00	243.00	1.10	0.10	47.00	145.00	13.90	7.30	3.40
			87.00	45.00	369.00	1.50	0.20	36.00	112.00	13.90	7.10	3.50
		60.00	39.00	129.00	1.50	0.30	46.00	144.00	14.30	8.10	3.80	
	28th Day	♀	27.00	15.00	345.00	1.00	0.40	37.00	119.00	12.80	8.90	2.80
			30.00	18.00	186.00	1.30	0.30	42.00	104.00	13.90	6.80	3.00
			63.00	36.00	104.00	1.20	0.20	35.00	180.00	16.60	8.40	3.50
		♂	69.00	24.00	273.00	1.50	0.20	40.00	150.00	15.30	7.10	3.40
			54.00	15.00	276.00	1.60	0.10	56.00	138.00	16.30	6.70	3.50
			51.00	24.00	180.00	1.80	0.30	60.00	119.00	16.00	6.70	3.40
	93rd Day	♂	39.00	15.00	225.00	1.40	0.20	58.00	108.00	16.80	6.90	3.50
			12.00	84.00	69.00	1.30	0.20	34.00	134.00	12.90	6.50	3.40
			36.00	27.00	78.00	1.20	0.30	72.00	126.00	14.40	7.40	3.10
		♀	120.00	167.00	69.00	1.50	0.20	30.00	111.00	9.70	6.30	3.10
			48.00	24.00	93.00	1.20	0.10	35.00	96.00	11.00	6.10	3.20
			39.00	72.00	60.00	1.60	0.20	41.00	110.00	14.30	7.40	3.30
			66.00	103.00	87.00	1.60	0.30	31.00	145.00	12.80	7.10	3.00
			27.00	45.00	99.00	1.00	0.30	41.00	124.00	14.80	7.10	3.40
			30.00	39.00	72.00	1.50	0.30	32.00	111.00	13.10	6.60	2.90
27.00	26.00	84.00	2.00	0.30	37.00	135.00	16.30	6.70	3.70			

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Table 6 (continued)

Group	Euthanization Day	Sex	ALT (U/L)	AST (U/L)	ALP (U/L)	Creatinine (mg/dL)	Total Bilirubin (mg/dL)	Urea (mg/dL)	Glucose (mg/dL)	Calcium (mg/dL)	Total Protein (g/dL)	Albumin (g/dL)	
Experimental Control (Intranasal)	14th Day	♂	27.00	30.00	150.00	0.90	0.30	34.00	114.00	14.40	7.30	3.40	
			57.00	45.00	324.00	1.50	0.20	39.00	139.00	16.80	8.20	3.60	
	28th Day	♀	24.00	29.00	114.00	1.20	0.30	52.00	143.00	13.80	7.50	2.90	
			51.00	17.00	246.00	1.60	0.30	57.00	143.00	14.10	7.00	3.10	
		♂	75.00	36.00	408.00	1.70	0.20	53.00	123.00	16.70	7.10	3.70	
			75.00	24.00	231.00	1.40	0.20	52.00	126.00	15.50	7.60	3.70	
		♀	42.00	15.00	165.00	1.40	0.30	29.00	136.00	15.30	7.10	3.60	
			24.00	9.00	153.00	1.10	0.30	19.00	137.00	15.70	7.10	3.50	
		93rd Day	♂	21.00	33.00	231.00	1.90	0.30	42.00	201.00	13.80	5.80	3.00
				36.00	79.00	102.00	1.80	0.20	46.00	99.00	12.10	6.20	3.00
				51.00	21.00	90.00	1.20	0.20	33.00	106.00	13.30	6.20	3.20
				87.00	99.00	96.00	1.60	0.30	42.00	98.00	10.30	5.10	2.60
			♀	159.00	78.00	120.00	1.40	0.20	36.00	100.00	11.50	7.70	2.60
				57.00	15.00	84.00	1.70	0.20	51.00	117.00	15.20	6.00	3.50
				91.00	102.00	30.00	1.30	0.20	65.00	114.00	13.00	8.10	2.70
				35.00	27.00	126.00	1.30	0.30	44.00	89.00	11.50	5.70	2.80
♂	105.00	51.00	105.00	1.60	0.30	38.00	97.00	11.60	6.00	2.70			
	42.00	24.00	180.00	1.60	0.30	40.00	97.00	10.80	4.90	2.60			
♀	48.00	30.00	96.00	2.40	0.30	43.00	131.00	16.90	7.10	3.60			

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Table 6 (continued)

Group	Euthanization Day	Sex	ALT (U/L)	AST (U/L)	ALP (U/L)	Creatinine (mg/dL)	Total Bilirubin (mg/dL)	Urea (mg/dL)	Glucose (mg/dL)	Calcium (mg/dL)	Total Protein (g/dL)	Albumin (g/dL)	
Experimental Control (Oral)	14th Day	♂	105.00	69.00	165.00	1.20	0.20	26.00	110.00	12.30	7.10	3.20	
			27.00	36.00	273.00	1.60	0.30	38.00	118.00	15.20	7.00	3.70	
		♀	39.00	30.00	186.00	1.60	0.30	50.00	118.00	14.30	7.20	3.20	
			33.00	29.00	189.00	1.40	0.20	47.00	134.00	14.40	6.70	3.10	
	28th Day	♂	63.00	24.00	204.00	1.50	0.20	51.00	129.00	15.30	6.70	3.50	
			24.00	15.00	435.00	1.10	0.10	47.00	129.00	14.00	7.90	3.50	
		♀	27.00	12.00	303.00	1.40	0.30	42.00	108.00	15.50	5.90	3.30	
			39.00	18.00	336.00	1.10	0.20	36.00	114.00	15.20	6.10	3.10	
	93rd Day	♂		48.00	9.00	207.00	1.30	0.30	48.00	111.00	15.00	6.80	3.50
				84.00	81.00	123.00	2.00	0.30	34.00	182.00	16.60	7.30	3.80
		♀		48.00	84.00	93.00	1.50	0.30	60.00	101.00	14.80	7.70	3.70
				90.00	105.00	165.00	1.10	0.20	60.00	111.00	13.30	9.10	2.90
				30.00	84.00	21.00	0.90	0.10	33.00	125.00	13.40	7.40	3.10
				42.00	141.00	87.00	1.70	0.20	45.00	219.00	14.50	7.10	3.50
				18.00	87.00	87.00	1.90	0.10	52.00	119.00	14.00	6.70	3.10
				51.00	51.00	144.00	1.40	0.20	36.00	113.00	13.20	6.00	2.90
				60.00	42.00	198.00	1.30	0.20	32.00	117.00	13.10	5.80	2.90
				13.00	15.00	105.00	1.70	0.20	40.00	125.00	16.50	7.90	3.80
			18.00	27.00	96.00	1.60	0.30	38.00	103.00	9.90	5.40	2.50	

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Table 6 (continued)

Group	Euthanization Day	Sex	ALT (U/L)	AST (U/L)	ALP (U/L)	Creatinine (mg/dL)	Total Bilirubin (mg/dL)	Urea (mg/dL)	Glucose (mg/dL)	Calcium (mg/dL)	Total Protein (g/dL)	Albumin (g/dL)
Prophylactic Dose (PD) Intra-Nasal	14th Day	♂	18.00	48.00	174.00	1.40	0.20	35.00	108.00	13.80	7.30	3.30
			42.00	18.00	132.00	1.00	0.30	112.00	147.00	12.90	8.60	3.10
			60.00	27.00	216.00	1.80	0.40	53.00	139.00	14.20	7.30	3.60
	28th Day	♀	30.00	24.00	117.00	1.20	0.20	59.00	118.00	15.30	9.20	3.30
			33.00	29.00	192.00	1.30	0.20	43.00	122.00	13.10	7.30	3.00
			45.00	20.00	375.00	1.40	0.20	45.00	115.00	15.30	8.30	3.60
		♀	72.00	30.00	198.00	1.40	0.10	45.00	137.00	16.10	7.20	3.70
			24.00	18.00	204.00	1.30	0.40	33.00	94.00	16.50	7.20	3.60
			42.00	18.00	231.00	1.60	0.20	39.00	101.00	15.00	6.80	3.40
	93rd Day	♂	36.00	15.00	168.00	1.50	0.20	44.00	109.00	15.10	5.90	3.30
			33.00	12.00	78.00	1.30	0.10	32.00	104.00	14.00	6.40	3.00
			63.00	33.00	105.00	1.60	0.20	27.00	116.00	15.50	7.60	3.20
		♀	64.00	24.00	102.00	1.30	0.30	26.00	127.00	16.20	7.40	3.80
			84.00	27.00	141.00	1.60	0.30	32.00	95.00	11.40	5.40	2.60
			42.00	78.00	72.00	1.10	0.30	43.00	114.00	14.20	7.70	3.30
			51.00	141.00	42.00	1.40	0.30	69.00	125.00	12.40	8.20	3.00
			15.00	78.00	60.00	1.70	0.20	42.00	115.00	14.40	6.90	3.40
			30.00	12.00	107.00	1.60	0.30	40.00	117.00	15.80	6.30	3.40
99.00	48.00	258.00	1.60	0.40	42.00	89.00	10.80	6.10	2.50			

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Table 6 (continued)

Group	Euthanization Day	Sex	ALT (U/L)	AST (U/L)	ALP (U/L)	Creatinine (mg/dL)	Total Bilirubin (mg/dL)	Urea (mg/dL)	Glucose (mg/dL)	Calcium (mg/dL)	Total Protein (g/dL)	Albumin (g/dL)
Prophylactic Dose (PD) Oral	14th Day	♂	33.00	27.00	378.00	1.30	0.20	45.00	137.00	16.40	8.50	3.60
			27.00	21.00	252.00	1.40	0.20	54.00	101.00	13.60	6.20	3.50
			27.00	27.00	255.00	1.50	0.20	34.00	129.00	16.50	9.60	3.80
	28th Day	♀	42.00	29.00	219.00	1.40	0.10	40.00	114.00	14.90	7.90	3.30
			33.00	16.00	321.00	1.40	0.20	53.00	131.00	13.20	6.80	2.80
			39.00	18.00	183.00	1.10	0.20	45.00	121.00	15.90	7.30	3.60
		♂	21.00	21.00	195.00	1.20	0.10	29.00	132.00	16.20	7.80	3.60
			69.00	9.00	297.00	1.10	0.30	38.00	117.00	15.70	6.60	3.30
			57.00	15.00	216.00	1.30	0.20	39.00	118.00	15.10	5.60	3.20
	93rd Day	♂	36.00	12.00	210.00	1.50	0.10	46.00	108.00	15.10	5.70	3.00
			81.00	24.00	78.00	1.40	0.30	37.00	107.00	10.90	5.20	2.70
			48.00	27.00	114.00	1.20	0.30	45.00	99.00	10.00	5.20	2.70
		♀	84.00	60.00	96.00	1.90	0.30	39.00	116.00	14.80	6.30	3.50
			78.00	108.00	297.00	1.80	0.20	32.00	115.00	12.50	6.20	2.90
			33.00	30.00	48.00	1.50	0.20	34.00	107.00	13.50	6.80	2.90
			30.00	69.00	39.00	1.10	0.30	25.00	114.00	12.30	6.90	2.60
			18.00	15.00	156.00	1.70	0.20	40.00	125.00	15.40	6.40	3.40
			24.00	29.00	102.00	1.90	0.20	64.00	143.00	15.30	6.90	3.60
	36.00	81.00	45.00	1.10	0.30	41.00	114.00	13.80	7.60	3.10		
	21.00	15.00	108.00	1.40	0.30	35.00	98.00	11.00	5.20	2.60		

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Table 6 (continued)

Group	Euthanization Day	Sex	ALT (U/L)	AST (U/L)	ALP (U/L)	Creatinine (mg/dL)	Total Bilirubin (mg/dL)	Urea (mg/dL)	Glucose (mg/dL)	Calcium (mg/dL)	Total Protein (g/dL)	Albumin (g/dL)
Average Dose (AD) Intra-Nasal	14th Day	♂	60.00	30.00	291.00	1.50	0.30	48.00	123.00	14.70	7.60	3.20
			33.00	16.00	138.00	0.70	0.40	103.00	109.00	13.00	8.30	2.50
			15.00	23.00	195.00	1.10	0.20	39.00	128.00	13.80	6.30	2.90
	28th Day	♀	39.00	14.00	126.00	1.00	0.30	68.00	102.00	14.30	9.10	3.20
			27.00	14.00	168.00	1.10	0.20	52.00	134.00	14.30	7.50	3.20
			54.00	33.00	264.00	1.60	0.10	46.00	116.00	15.60	7.50	3.80
		♂	51.00	21.00	207.00	1.30	0.20	60.00	128.00	15.00	7.30	3.60
			102.00	30.00	405.00	1.30	0.10	33.00	105.00	14.90	5.60	3.10
			36.00	12.00	246.00	1.40	0.20	41.00	107.00	15.00	6.30	3.20
	93rd Day	♀	36.00	15.00	204.00	1.30	0.30	39.00	115.00	15.80	6.60	3.40
			51.00	101.00	54.00	1.40	0.20	42.00	110.00	13.70	8.90	3.10
			12.00	78.00	78.00	1.90	0.20	59.00	114.00	12.60	7.90	3.10
		♂	69.00	39.00	210.00	1.50	0.30	33.00	111.00	16.40	7.20	3.70
			60.00	21.00	138.00	1.50	0.30	33.00	109.00	16.00	6.30	3.60
			42.00	21.00	108.00	1.40	0.20	30.00	109.00	11.40	5.30	2.60
			102.00	49.00	144.00	1.10	0.40	32.00	96.00	13.20	8.00	3.10
			66.00	36.00	114.00	1.50	0.50	41.00	119.00	14.30	6.90	3.40
			48.00	21.00	72.00	1.80	0.20	40.00	182.00	15.60	6.30	3.40
	♀	30.00	6.00	81.00	1.60	0.30	46.00	130.00	11.20	6.40	2.80	
		78.00	48.00	309.00	1.70	0.40	45.00	113.00	11.00	5.40	2.70	

Table 7.1
Organ Weights of rats Euthanized on 15th Day of Post-Exposure of recombinant HPV vaccine.

Group	Time Point	Sex	Brain (g)	Heart (g)	Kidney (L & R) (g)	Liver (g)	Lungs (L & R) (g)	Spleen (g)	Testis (L & R) (g)	
Vehicle Control	15th Day	♂	1.7	0.9	1.4	5.6	1.3	0.4	2.1	
			1.8	0.9	1.6	6.4	1.1	0.2	3.7	
			1.6	0.8	1.5	5.9	1.5	0.3	2.5	
		♀	1.8	0.8	1.5	4.9	1.2	0.4	NA	
			1.5	0.8	1.5	5.4	1.5	0.3	NA	
			1.7	0.7	1.6	5.5	1.3	0.4	NA	
Experimental Control	IN	♂	1.5	1.0	1.5	5.5	1.1	0.3	3.4	
			1.6	1.1	1.9	7.2	1.2	0.3	3.7	
			1.5	0.7	1.7	5.3	1.8	0.4	3.8	
		♀	1.7	0.7	1.4	4.9	1.4	0.4	NA	
			1.7	0.7	1.4	4.6	1.1	0.4	NA	
			1.7	0.8	1.6	5.0	1.1	0.4	NA	
	Oral	15th Day	♂	1.7	0.9	1.9	6.1	1.6	0.4	3.3
				1.6	0.7	1.5	5.9	1.3	0.3	3.1
				1.8	0.8	1.5	4.9	1.2	0.3	3.7
			♀	1.7	0.8	1.5	5.5	1.2	0.3	NA
				1.6	0.9	1.5	6.1	1.5	0.4	NA
				1.4	0.9	1.6	6.2	1.1	0.4	NA
Prophylactic Dose (PD)	IN	♂	1.8	0.9	1.5	6.5	1.5	0.4	3.9	
			1.8	1.0	1.6	7.0	1.5	0.5	2.6	
			1.7	1.1	1.8	6.1	1.4	0.4	4.6	
		♀	1.5	0.9	1.6	4.7	1.5	0.6	NA	
			1.9	0.8	1.4	5.4	1.3	0.4	NA	
			1.5	1.1	1.8	5.9	1.4	0.4	NA	
	Oral	15th Day	♂	1.8	1.1	1.8	6.8	1.2	0.5	3.6
				1.8	1.0	1.9	6.3	1.4	0.3	5.4
				1.8	1.1	2.2	6.5	2.0	0.4	4.4
			♀	1.6	1.0	1.9	5.7	1.4	0.4	NA
				1.8	1.4	2.1	6.6	1.5	0.5	NA
				1.8	0.8	1.8	6.0	1.4	0.4	NA
Average Dose (IN)	15th Day	♂	1.6	1.1	1.7	5.5	1.8	0.4	4.1	
			1.8	1.1	1.9	6.4	1.4	0.4	3.8	
			1.9	1.1	2.4	8.2	1.7	0.5	5.8	
		♀	1.7	1.1	1.8	5.3	1.7	0.5	NA	
			1.7	1.1	1.8	5.8	1.4	0.5	NA	
			1.8	0.6	1.5	4.5	1.0	0.4	NA	

L & R: Left and Right Kidneys, Lungs and Testis; NA: Not Applicable.

The [Table 9](#) data consist of bone marrow micronucleus levels in rats administered with rSt.HPV expressing HPV 16 and 18 L1 proteins as part of sub-chronic testing of vaccine. Similarly the [Table 10](#) comprised of data of bone marrow micronucleus of rabbits used for sub-chronic testing of rSt.HPV vaccine.

The immune response in terms of specific IgG levels against HPV 16 L1 and 18 L1 proteins were given in [Table 11](#). Similarly, the allergenicity of rSt.HPV expressing HPV 16 and 18 L1 proteins, if any assessed in terms of specific IgE levels against HPV 16 L1 and 18 L1 proteins were given in [Table 12](#).

2. Experimental Design, Materials and Methods

The nonclinical efficacy and safety/toxicology of recombinant *S. typhi* Ty21a expressing HPV 16 and 18 L1 proteins was generated previously [1]. Selection of animals species, strain, sex, age and weight of animals were illustrated in the research article published in vaccine journal [1]. The animals were obtained from National Centre for Laboratory Animals Sciences (ICMR-NIN), Hyderabad. Data of current article collected from rats and rabbits administered with attenuated

Table 7.2

Organ Weights of rats Euthanized on 29th Day of Post-Exposure of recombinant HPV vaccine.

Group	Time Point	Sex	Brain (g)	Heart (g)	Kidney (L & R) (g)	Liver (g)	Lungs (L & R) (g)	Spleen (g)	Testis (L & R) (g)	
Vehicle Control	29th Day	♂	1.8	0.9	1.6	6.6	1.8	0.4	3.8	
			1.5	1.2	1.8	7.2	1.6	0.5	2.8	
			1.8	1.4	2.2	7.5	3.0	0.6	4.8	
		♀	1.9	0.8	1.6	5.9	1.9	0.4	NA	
			1.6	0.9	1.5	5.7	1.6	0.5	NA	
			1.4	0.6	1.4	4.5	1.6	0.3	NA	
Experimental Control	IN	♂	4.3	1.0	1.6	5.3	1.2	0.2	4.5	
			1.9	0.8	1.7	6.9	1.3	0.4	2.9	
			1.8	0.9	1.6	6.3	1.6	0.2	3.2	
		♀	1.7	1.0	1.6	5.4	3.0	0.3	NA	
			1.8	0.7	1.6	4.9	1.3	0.2	NA	
			1.7	0.9	2.0	6.7	1.4	0.5	NA	
	Oral	29th Day	♂	1.4	1.1	1.8	7.1	2.6	0.4	3.9
				1.8	1.2	1.9	6.2	1.9	0.6	2.9
				1.6	1.2	2.1	6.8	1.4	0.5	4.4
			♀	1.8	0.9	1.6	4.9	1.2	0.3	NA
				1.4	0.8	1.7	5.1	1.7	1.3	NA
				1.9	1.1	1.9	6.9	1.4	0.4	NA
Prophylactic Dose (PD)	IN	♂	1.6	1.1	2.2	5.8	1.8	1.5	3.9	
			1.9	1.1	1.9	8.1	1.7	0.6	5.5	
			1.8	1.3	2.5	9.3	1.8	0.5	4.2	
		♀	1.7	0.8	1.5	5.4	1.3	0.4	NA	
			1.5	1.0	1.6	5.5	1.7	0.3	NA	
			1.7	0.8	1.8	5.2	1.7	0.4	NA	
	Oral	29th Day	♂	1.8	0.9	1.6	6.4	1.1	0.3	4.9
				1.8	1.0	1.6	6.5	1.4	0.4	3.5
				1.7	1.2	1.7	6.8	1.7	0.4	5.1
			♀	1.4	0.8	1.7	6.4	1.4	0.4	NA
				1.4	1.0	1.8	6.6	1.7	0.5	NA
				1.8	1.0	1.6	6.6	1.4	0.4	NA
Average Dose (IN)	29th Day	♂	2.0	1.2	2.2	6.9	1.4	0.4	5.2	
			1.6	0.9	2.0	6.4	2.1	0.5	3.6	
			1.9	1.0	1.6	6.3	1.8	0.3	4.6	
		♀	1.7	0.8	1.4	5.6	1.3	0.4	NA	
			1.7	1.0	1.7	5.5	1.6	0.3	NA	
			1.7	1.1	1.7	5.7	1.8	0.6	NA	

L & R: Left and Right Kidneys, Lungs and Kidneys; NA: Not Applicable.

S. typhi Ty21a expressing the HPV 16 and 18 L1 proteins as vaccine candidate. Intended clinical application of test compound is 'oral route', in view of non-colonisation of attenuated *S. typhi* Ty21a in laboratory animals, the sub-chronic toxicity of vaccine candidate was tested through oral route (as per regulatory guidelines) and innovative intranasal route [2, 3]. Since the test compounds is recombinant vaccine, due approvals from Institutional Biosafety Committee (IBSC) and Review Committee on Genetic Manipulation (RCGM), Department of Biotechnology (DBT), India were obtained for sub-chronic toxicity testing as per Schedule Y of Drug Controller General of India (DCGI) [4]. The prophylactic dose for Sprague Dawley (SD) rats (PD: 0.18×10^9 CFU/kg) and New Zealand White (NZW) rabbits (PD: 0.09×10^9 CFU/kg) were derived using pharmacological conversion factor [5] from adult human clinical dose (2×10^9 CFU/kg/70 kg). The prophylactic doses were administered through oral and intranasal routes to rats (100 µl) and rabbits (200 µl), whereas the average dose ($5 \times$ PD) was administered to rats (AD: 0.9×10^9 CFU/kg) and rabbits (AD: 0.45×10^9 CFU/kg) through intranasal routes only.

The repeated dose effect of test compound was assessed through successive exposures on Day 1, Day 3 and Day 5 with specified routes. The effect of vector i.e. attenuated *S. typhi* Ty21a, was assessed in rats and rabbits by administration through oral and intranasal routes and represented as Experimental control groups. Similarly, the effect of vehicle i.e. phosphate buffer

Table 7.3
Organ Weights of rats Euthanized on 93rd Day of Post-Exposure of recombinant HPV vaccine.

Group	Time Point	Sex	Brain (g)	Heart (g)	Kidney (L & R) (g)	Liver (g)	Lungs (L & R) (g)	Spleen (g)	Testis (L & R) (g)			
Vehicle Control	93rd Day	♂	1.6	1.4	1.2	9.9	2.2	0.6	5			
			1.2	1.1	2.2	7.4	1.7	0.4	4.4			
			1.8	0.9	1.8	7.6	1.5	0.4	3.2			
			1.7	1.3	2.2	8.9	2.7	0.5	4.4			
			1.8	1.2	2.2	8.3	2.9	0.6	5.7			
			1.9	1.5	2.0	8.7	2.3	0.5	4.6			
			1.9	0.9	1.9	5.9	1.2	0.4	NA			
		♀	1.9	1	1.9	6.1	1.6	0.5	NA			
			1.6	1.1	1.5	5.9	1.8	0.3	NA			
			1.4	0.8	1.9	6.1	2.3	0.5	NA			
			1.9	1.2	1.9	6.9	2.0	0.5	NA			
			1.9	1.1	2.0	7.0	2.3	0.4	NA			
			Experimental Control	93rd Day	♂	1.9	1.4	2.3	8.4	1.7	0.4	4.8
						1.8	1.1	2.5	8	1.9	0.4	3.8
2.0	1	2.4				6.8	1.6	0.4	4.4			
1.8	1.2	2.3				8	2.1	0.5	5.2			
1.8	0.8	2.3				8	2	0.4	4.6			
1.7	1.1	2.6				8.5	2	0.5	5.2			
1.8	1.1	2				6.9	2.3	0.7	NA			
♀	1.6	1.2			1.7	6.2	2.1	0.5	NA			
	2.2	1			2.1	5.8	2.1	0.6	NA			
	1.8	1.1			1.7	6.2	1.7	0.4	NA			
	1.7	1.1			1.7	6.3	2.1	0.5	NA			
	1.7	1.2			2.1	8.6	1.8	0.3	4.9			
	1.8	1.4			2.3	9.4	1.9	0.8	6.9			
	1.9	1.5			2.5	8.7	2.0	0.6	5.4			
Oral	93rd Day	♂	2.0	1.9	2.7	10.6	2.1	0.6	6.0			
			2.0	1.3	2.2	8.7	1.8	0.5	5.1			
			1.5	1.4	2.9	10.2	2.0	0.5	6.4			
			1.4	1	1.7	6.6	1.8	0.3	NA			
			2.2	0.9	1.8	7	1.5	0.6	NA			
			1.5	1.2	1.8	6.9	2.2	0.2	NA			
			1.9	1.0	2.1	7.2	1.7	0.6	NA			
		♀	1.7	1.0	1.8	6.1	1.9	0.4	NA			
			1.9	1.2	2.1	8.0	1.7	0.6	NA			
			Prophylactic Dose (PD)	93rd Day	♂	1.6	2.5	2.9	9.8	2.8	0.7	5.2
						1.6	1.4	2.4	9.1	1.8	0.5	6.4
						1.6	2.2	2.3	9.2	1.9	0.4	6.0
						2.0	1.6	2.8	8.4	2.7	0.6	5.2
						1.6	1.0	2.4	8.8	2.3	0.5	5.3
1.8	1.4	2.2				8.3	1.7	0.5	5.2			
1.8	1.1	2.1				7.4	2.0	0.4	NA			
♀	1.6	1.0			1.7	6.0	1.7	0.3	NA			
	1.8	0.8			2.0	8.3	2.1	0.6	NA			
	1.5	0.8			1.8	6.7	1.8	0.4	NA			
	Oral	93rd Day			♂	1.7	1.6	1.9	8.1	2.1	0.6	4.5
						1.9	1.2	2.3	7.9	1.7	0.5	5.2
						1.7	1.8	2.3	11.4	1.7	0.8	3.8
						1.5	1.1	2.2	7.1	1.9	0.4	5.1
1.6			1.1	2.0		7.6	2.4	0.4	4.8			
2.0			1.6	2.3		7.6	2.2	0.4	4.7			
1.5			0.9	1.9		6.8	2.1	0.5	NA			
♀			1.7	0.7	1.8	6.5	1.3	0.5	NA			
			1.5	0.8	1.7	5.3	2.3	0.3	NA			
			1.7	0.9	1.7	7.3	1.5	0.5	NA			
			1.8	0.9	2.2	6.9	1.6	0.4	NA			
			1.9	1.4	1.7	5.5	1.8	0.3	NA			

(continued on next page)

Table 7.3 (continued)

Group	Time Point	Sex	Brain (g)	Heart (g)	Kidney (L & R) (g)	Liver (g)	Lungs (L & R) (g)	Spleen (g)	Testis (L & R) (g)
Average Dose (IN)	93rd Day	♂	1.8	1.1	1.7	7.5	2.9	0.4	4.5
			1.9	1.5	2.6	9.2	1.9	0.7	3.3
			1.8	1.5	2.2	8.8	2.0	0.6	4.8
			1.9	1.2	2.6	9.6	1.7	0.5	7.4
			1.7	1.2	2.4	8.1	2.1	0.4	3.4
		1.7	1.3	2.2	8.3	2.0	0.7	4.7	
		♀	1.7	1.0	1.8	6.7	1.6	0.4	NA
			1.9	1.0	2.0	7.5	2.5	0.6	NA
			1.7	0.9	1.8	7.1	1.6	0.5	NA
			1.7	1.1	1.9	6.8	2.0	0.5	NA
			1.8	1.2	1.6	5.5	1.8	0.4	NA
			1.6	1.1	1.7	6.6	2.0	0.4	NA

L & R: Left and Right Kidneys, Lungs and Testis; NA: Not Applicable.

Table 8.1

Organ Weights of rabbits Euthanized on 15th Day of Post-Exposure of recombinant HPV vaccine.

Group	Time Point	Sex	Brain (g)	Heart (g)	Kidney (L & R) (g)	Liver (g)	Lungs (L & R) (g)	Spleen (g)	Testis (L & R) (g)	
Vehicle Control	15th Day	♂	7.7	4.8	9.3	48.8	7.5	0.9	2.5	
			7.9	5.4	13.5	53.3	7.6	1.2	6.9	
			6.8	4.1	11.1	51.4	11.2	0.7	7.0	
		♀	9.2	6.8	13.4	52.8	9.4	1.1	NA	
			8.7	5.9	11.6	59.6	11.8	0.9	NA	
Experimental Control	IN	♂	7.5	4.8	11.4	52.7	8.7	1.0	3.1	
			9.0	6.6	13.0	63.7	15.7	1.6	6.5	
			7.7	5.3	10.9	54.3	8.8	1.0	NA	
		♀	9.5	5.5	12.1	67.2	10.4	1.9	NA	
			9.3	7.5	12.9	84.6	9.9	2.6	5.4	
	Oral	15th Day	♂	8.9	7.0	11.9	58.3	22.5	1.7	6.9
				8.3	8.2	12.9	45.9	11.6	1.2	NA
				7.8	6.6	11.7	65.7	8.7	0.8	NA
			♀	9.4	6.0	16.8	67.8	11.7	1.8	8.9
				8.5	8.4	12.1	41.4	7.5	0.6	1.9
Prophylactic Dose (PD)	IN	♂	9.0	5.1	10.2	40.6	8.8	1.0	7.8	
			6.4	5.5	8.6	31.7	5.7	0.6	NA	
			8.1	9.1	14.6	57.8	11.8	1.3	NA	
		♀	8.8	7.8	11.0	57.8	8.8	0.8	5.1	
			7.7	7.1	10.3	43.8	10.3	0.7	5.9	
	Oral	15th Day	♂	7.4	4.3	11.3	42.4	6.9	0.5	5.1
				9.1	6.6	14.2	79.1	13.2	2.1	NA
				6.3	5.0	10.3	50.6	11.1	1.2	NA
			♀	7.6	7.0	12.7	58.9	8.8	1.0	4.9
				7.3	4.5	12.1	36.7	6.6	0.5	1.1
Average Dose (IN)	15th Day	♂	10.1	8.8	16.4	82.4	13.1	2.6	7.5	
			7.4	6.6	11.1	43.4	9.6	2.0	NA	
		♀	6.5	7.4	11.2	80.3	9.5	1.1	NA	

L & R: Left and Right Kidneys, Lungs and Testis; NA: Not Applicable.

saline (PBS), was assessed by administration through intranasal routes to rats and rabbits and represented as vehicle control groups. To unveil the test compound effect in relation with time was assessed by euthanizing 25% of animals on 15th day, another 25% animals on 29th Day and remaining animals on 93rd day of post-exposure of 1st dose. Blood was collected from retro-orbital plexus using microhematocrit capillaries (Fisher Scientific # 22-362,566) into K2EDTA tubes (BD Vacutainer) before euthanizing the animals, whereas vital organs were collected after euthanization. The body weights of animals were obtained periodically.

Table 8.2
Organ Weights of rabbits Euthanized on 29th Day of Post-Exposure of recombinant HPV vaccine.

Group	Time Point	Sex	Brain (g)	Heart (g)	Kidney (L & R) (g)	Liver (g)	Lungs (L & R) (g)	Spleen (g)	Testis (L & R) (g)
Vehicle Control	29th Day	♂	7.4	3.9	11.7	45.2	7.3	0.2	4.8
			9.3	8.9	16.0	60.7	9.7	1.2	7.0
		♀	6.5	5.0	11.8	51.4	10.9	0.8	NA
			7.1	4.5	9.4	41.4	8.1	0.9	NA
Experimental Control	IN	♂	9.3	6.5	12.8	58.0	11.9	1.2	NA
			7.3	6.2	11.6	63.6	13.6	0.6	7.7
			3.4	2.9	7.9	45.0	4.4	0.2	4.4
		♀	7.9	6.5	11.0	57.1	6.7	0.9	NA
			8.8	6.6	14.2	75.0	11.5	0.8	NA
			5.9	9.4	9.9	58.2	7.5	0.8	NA
	Oral	♂	8.3	6.0	13.7	61.8	12.1	0.6	5.0
			7.0	6.5	11.7	68.6	10.5	2.0	4.6
			8.4	6.7	11.3	55.8	8.0	0.8	NA
		♀	7.3	6.0	14.3	59.3	13.2	1.3	NA
			6.0	5.2	9.9	66.1	9.4	1.1	NA
			7.7	8.9	12.5	61.2	9.4	0.9	7.0
Prophylactic Dose (PD)	IN	♂	8.0	6.9	12.9	75.6	10.5	0.5	7.2
			8.9	7.9	11.9	62.5	8.3	1.3	NA
			8.5	4.9	14.2	63.9	10.3	1.5	NA
		♀	8.5	4.7	10.1	48.5	12.3	1.0	NA
			8.6	3.9	10.1	45.1	5.8	0.4	4.8
			8.0	6.0	13.5	79.1	12.9	1.1	6.9
	Oral	♂	7.9	5.1	14.1	61.2	9.4	0.7	NA
			6.6	6.3	11.2	68.6	7.9	1.1	NA
			8.5	4.7	10.5	62.2	9.4	0.9	NA
		♀	8.0	5.0	12.0	62.7	9.5	0.8	7.0
			8.6	6.3	12.8	67.1	10.2	1.1	5.2
			7.7	4.1	9.5	49.0	8.6	0.8	NA
Average Dose (IN)	29th Day	♂	7.3	5.7	12.8	73.6	9.5	1.9	NA
			8.0	4.5	10.0	54.0	8.1	0.8	NA
		♀	8.0	5.0	12.0	62.7	9.5	0.8	7.0
			8.6	6.3	12.8	67.1	10.2	1.1	5.2

L & R: Left and Right Kidneys, Lungs and Testis; NA: Not Applicable.

Blood samples were analysed for haemoglobin, indices of red blood cells, differential leucocyte count and total leucocyte count using automated blood cell counter as per the manufacturer’s instructions and guidelines (Serono Baker System 9120 CP+, USA) [6]. The biochemical profile viz. ALT, AST, ALP, creatinine, total bilirubin, urea, glucose, calcium, total protein and albumin levels were determined in serum samples using ACE™ clinical autoanalyzer (Model Ace Alera). Whereas, the weights of vital organs were recorded using analytical balance (Sartorius, SECURA125–10BR). The genotoxic effect of rSt.HPV expressing HPV 16 and 18 L1 proteins, if any were determined in rats and rabbits used for sub-chronic toxicity testing through bone marrow micronucleus assay. Mice were used to determine the immune response in terms of specific IgG levels and allergenicity in terms of specific IgE levels were assessed using standard ELISA method. The raw data of all the animals euthanized at different time points were compiled and computed according to the groups.

Table 8.3

Organ Weights of rabbits Euthanized on 93rd Day of Post-Exposure of recombinant HPV vaccine.

Group	Time Point	Sex	Brain (g)	Heart (g)	Kidney (L & R) (g)	Liver (g)	Lungs (L & R) (g)	Spleen (g)	Testis (L & R) (g)
Vehicle Control	93rd Day	♂	7.9	5.4	10.9	65.3	7.9	0.8	7.4
			8.1	5.0	8.6	51.5	7.7	0.8	6.6
			7.9	7.7	8.3	62.6	10.3	1.3	5.8
			8.5	5.6	11.0	61.5	8.6	0.9	6.8
			8.1	5.1	10.1	41.9	9.1	0.5	7.5
			8.6	4.9	10.2	51.1	11.5	0.6	NA
		♀	8.8	6.6	11.2	54.0	12.3	1.3	NA
			7.1	5.1	11.3	59.8	7.8	1.2	NA
			9.5	5.4	11.1	54.6	11.3	1.6	NA
			8.9	6.9	10.9	51.9	11.8	1.3	NA
			8.1	5.0	9.5	54.3	10.2	1.1	8.2
			8.3	4.8	8.7	47.7	11.1	0.7	9.5
Experimental Control	93rd Day	♂	8.1	5.0	9.5	54.3	10.2	1.1	8.2
			8.3	4.8	8.7	47.7	11.1	0.7	9.5
			8.1	5.5	10.4	54.5	8.9	0.4	8.8
			9.3	7.2	14.0	81.0	10.9	1.6	7.8
			8.9	6.4	9.7	55.5	13.2	0.9	9.7
			9.3	9.2	14.7	65.1	10.7	1.0	3.7
		♀	8.6	4.9	12.1	52.1	8.7	1.4	NA
			8.3	4.9	8.8	45.9	8.7	1.1	NA
			9.1	5.5	10.3	45.4	9.4	1.0	NA
			8.3	8.6	9.8	60.2	10.9	1.7	NA
			7.9	5.4	13.1	57.0	8.5	0.9	5.5
			8.6	8.6	13.7	64.0	12.7	0.7	7.3
Prophylactic Dose (PD)	93rd Day	♂	9.0	5.5	10.1	55.1	8.8	0.6	7.9
			9.5	6.0	9.3	57.6	6.0	1.5	9.0
			6.7	4.5	11.5	55.5	12.5	1.1	5.5
			8.5	5.7	10.6	66.6	10.4	10.3	NA
			10.1	6.1	13.0	55.4	10.5	0.9	NA
			8.1	6.4	11.5	60.7	12.1	1.7	NA
		♀	9.0	4.5	10.3	49.6	8.5	0.8	NA
			8.8	4.8	12.5	52.8	12.6	1.0	NA
			8.1	6.6	12.1	66.2	11.7	0.9	8.7
			7.2	5.4	9.6	44.3	8.9	0.7	5.4
			8.1	7.1	11.0	63.1	13.2	0.9	9.0
			9.0	4.9	11.2	56.8	10.9	1.1	6.6
Average Dose (IN)	93rd Day	♂	9.2	5.2	11.6	55.4	11.9	0.8	8.3
			9.4	6.1	13.1	65.2	10.8	2.2	NA
			6.2	5.1	9.8	52.6	10.6	1.2	NA
			5.3	4.1	9.0	33.7	7.2	0.7	NA
			9.2	5.3	11.9	49.2	10.7	1.3	NA
			9.5	5.0	10.2	58.7	9.7	1.1	5.6
		♀	8.9	5.8	12.5	64.5	13.8	0.6	8.6
			7.7	6.4	10.1	72.3	1.6	1.1	9.9
			7.4	6.9	10.3	59.6	11.3	0.9	8.7
			8.7	5.9	11.9	63.0	14.2	0.6	9.0
			6.9	5.7	12.3	57.3	11.0	0.7	NA
			9.0	6.3	13.3	73.0	10.8	0.8	NA
Average Dose (IN)	93rd Day	♂	8.1	5.1	8.4	40.4	9.2	1.2	NA
			9.8	5.7	10.2	45.7	9.8	9.2	NA
			9.3	6.8	11.8	60.8	10.7	1.1	NA
			8.4	4.8	10.0	62.1	11.2	0.9	7.9
			5.8	5.5	10.2	54.2	8.1	0.6	7.2
			8.1	6.3	11.4	66.3	16.2	1.1	5.8
		♀	9.3	5.1	11.4	56.7	10.5	1.1	7.3
			9.0	6.1	9.3	50.6	7.5	0.7	9.9
			8.2	5.6	17.5	77.3	16.0	3.2	NA
			8.2	8.3	9.2	52.1	13.0	1.5	NA
			7.8	5.4	10.8	54.0	9.5	1.3	NA
			9.0	5.6	9.4	76.0	8.6	0.8	NA
9.0	5.8	11.1	53.5	13.1	1.2	NA			

L & R: Left and Right Kidneys, Lungs and Testis; NA: Not Applicable.

Table 9

The data of Bone Marrow Micronucleus of rats exposed with rSt.HPV expressing HPV 16 and 18 L1 Proteins as part of Sub-chronic Testing.

Parameter	Euthanization Day	Sex	Vehicle Control (VC)	Experimental Control (EC)		Prophylactic Dose (PD)		Average Dose – Intra-Nasal (IN)
				Intra-Nasal (IN)	Oral	Intra-Nasal (IN)	Oral	
PCE per 200 NCE	15th Day	♂	0.59	1.06	0.74	0.78	0.79	0.81
			0.99	0.95	0.76	0.92	0.81	0.93
			0.74	0.89	0.74	0.96	0.87	0.97
		♀	1.03	0.99	0.91	1.04	1.01	0.94
			1.06	0.92	1.17	0.87	0.98	1.04
			1.10	0.96	1.06	0.91	0.92	0.77
	29th Day	♂	0.91	0.99	1.07	0.89	0.96	1.09
			0.84	1.17	0.97	0.97	1.05	1.06
			1.07	1.34	0.98	0.93	1.07	1.17
		♀	1.24	1.02	0.97	0.89	0.74	0.94
			1.09	1.06	0.92	0.92	0.82	0.88
			1.10	1.03	0.91	0.84	0.92	0.87
	93rd Day	♂	0.99	1.12	1.07	0.97	0.93	0.92
			0.97	1.17	1.06	0.96	0.87	0.74
			1.21	1.23	0.82	0.96	0.82	0.77
			1.16	1.05	0.88	0.96	0.91	0.82
			0.97	1.07	0.92	0.80	0.99	0.91
			0.74	1.06	0.91	0.86	0.71	0.96
		♀	0.97	1.06	1.31	1.17	1.05	0.98
			0.96	1.16	1.20	1.15	1.14	0.87
			1.13	1.12	1.14	1.09	0.74	0.91
			0.88	0.69	0.82	1.10	0.99	0.91
			0.09	0.74	0.80	-	0.92	0.67
			0.96	-	0.86	-	0.82	0.92
MNPCE per 2000PCE	15th Day	♂	0.60	1.40	0.70	1.20	1.70	1.30
			0.90	1.20	0.40	1.40	2.10	1.70
			0.50	0.80	0.60	1.50	1.60	1.90
		♀	0.60	0.30	0.70	0.70	1.40	0.70
			1.50	0.40	0.60	0.90	1.10	1.20
			0.50	0.20	0.50	1.20	1.60	0.80
	29th Day	♂	0.60	0.50	1.00	1.00	1.50	1.70
			0.70	0.50	1.20	1.20	0.90	1.60
			0.90	0.40	1.10	1.60	1.30	1.50
		♀	0.90	1.30	0.90	0.50	0.70	0.70
			0.70	1.00	0.10	0.90	0.90	1.20
			0.60	1.10	0.40	0.60	0.65	1.40
	93rd Day	♂	0.60	0.40	0.90	1.40	1.20	0.60
			0.90	0.70	1.05	1.30	1.20	1.50
			0.70	0.30	0.50	1.70	1.30	1.60
			0.50	0.30	0.60	1.40	1.10	1.20
			0.50	0.60	0.70	1.20	1.00	2.10
			0.20	0.70	0.80	1.40	1.20	1.40
		♀	1.30	0.60	1.30	1.60	0.50	0.70
			1.20	0.50	0.90	1.50	0.60	1.40
			1.00	1.20	0.85	1.30	1.30	1.90
			1.20	1.30	1.10	1.00	1.40	1.30
			1.10	1.20	0.60	-	1.70	1.20
			1.00	-	0.50	-	1.60	1.40

Table 10

Bone Marrow Micronucleus data of rabbits used for sub-chronic testing of rSt.HPV expressing HPV 16 and 18 L1proteins.

Parameter	Euthanization Day	Sex	Vehicle Control (VC)	Experimental Control (EC)		Prophylactic Dose (PD)		Average Dose – Intra-Nasal (IN)	
				Intra-Nasal (IN)	Oral	Intra-Nasal (IN)	Oral		
PCE per 200 NCE	15th Day	♂	212	216	198	174	162	176	
			241	236	186	168	182	167	
			228	–	–	194	190	184	
	29th Day	♀	196	192	158	198	194	201	
			182	188	147	182	196	206	
			216	202	185	168	206	204	
		♂	228	198	192	194	207	202	
			238	194	184	198	168	164	
			248	186	205	174	176	182	
	93rd Day	♂	214	192	202	184	145	174	
			199	134	146	168	186	194	
			196	148	167	148	146	156	
		♀	146	146	120	194	128	122	
			128	165	182	142	194	130	
			156	134	174	192	164	166	
		♂	206	174	188	162	208	184	
			172	216	146	160	158	163	
			171	203	158	164	183	194	
	MNPCE per 2000PCE	15th Day	♂	207	142	143	122	147	164
				176	144	132	–	132	188
				24	30	30	21	22	28
29th Day		♀	34	34	42	34	26	20	
			32	–	–	28	22	27	
			16	22	32	42	28	38	
		♂	18	20	34	30	24	34	
			38	42	24	28	26	34	
			48	34	21	24	30	48	
93rd Day		♀	18	14	30	32	18	10	
			34	34	34	30	10	12	
			12	32	42	30	16	16	
		♂	17	14	17	18	22	12	
			16	15	18	10	26	12	
			20	10	12	34	12	10	
	♀	10	10	20	16	13	18		
		26	10	14	12	18	18		
		8	24	6	20	32	42		
34		20	11	28	16	32			
22		84	26	28	20	18			
34		34	24	30	13	14			
14	21	20	–	18	26				

Table 11
Specific IgG levels against rSt.HPV 16 and 18 expressing L1 proteins in mice.

Route of Administration	Euthanization Day	Anti-HPV 16 L1 IgG				Anti-HPV 18 IgG			
		Vehicle Control	OVA	1x HPV	5x HPV	Vehicle Control	OVA	1x HPV	5x HPV
Intra-Nasal Route	0th Day	0.0762	0.1293	0.0636	0.0679	0.0732	0.1293	0.0594	0.0845
		0.0569	0.1343	0.0624	0.0643	0.0787	0.1343	0.0662	0.0812
		0.0614	0.1403	0.0531	0.0515	0.0715	0.1403	0.0821	0.0626
		0.074	-	0.0597	0.0655	0.0771	-	0.092	0.0812
		0.062	-	0.06	0.0633	0.0782	-	0.0741	0.0667
	28th Day	0.0721	-	0.0569	0.064	0.1179	-	0.0904	0.07
		0.053	0.1676	0.0628	0.0948	0.1315	0.1676	0.0789	0.8093
		0.0794	0.1946	0.0883	0.0784	0.1347	0.1946	0.1283	0.2068
		0.0758	0.2138	0.08	0.0794	0.1512	0.2138	0.141	0.337
		0.0884	-	0.0759	0.089	0.1551	-	0.121	0.6167
		0.0762	-	0.0814	-	0.1253	-	0.1191	-
		-	-	0.0816	-	-	-	0.1111	-
		0.1193	0.2913	0.0499	0.5304	0.1094	0.2913	0.116	0.6343
	56th Day	0.1364	0.3678	0.0972	0.1214	0.1498	0.3678	0.1138	0.6662
		0.1087	0.2602	0.1846	0.307	0.1268	0.2602	0.1577	0.874
		0.138	0.4617	0.0937	0.1482	0.1554	0.4617	0.1067	0.8688
		0.1319	0.5098	0.0466	-	0.1417	0.5098	0.1157	-
		-	0.4197	0.0922	-	-	0.4197	0.1201	-
		0.1603	0.543	0.1942	1.2392	0.2261	0.543	0.2291	0.6683
		0.2028	0.5376	0.1221	0.1473	0.2245	0.5376	0.2508	0.5359
	63rd Day	0.1639	0.5036	0.1626	0.7843	0.2033	0.5036	0.1802	1.0143
		0.1445	0.5257	0.1557	0.1856	0.1712	0.5257	0.5284	1.0121
		0.1666	0.6643	0.1434	-	0.2724	0.6643	0.1877	-
		-	-	0.1387	-	-	-	0.2256	-
		0.1436	0.497	0.1238	0.6433	0.1171	0.497	0.1185	0.9733
		0.0989	0.6288	0.1178	0.1627	0.1253	0.6288	0.1044	0.9769
	78th Day	-	0.4594	0.1685	-	-	0.4594	0.1623	-

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Table 11 (continued)

Route of Administration	Euthanization Day	Anti-HPV 16 L1 IgG				Anti-HPV 18 IgG			
		Vehicle Control	OVA	1x HPV	5x HPV	Vehicle Control	OVA	1x HPV	5x HPV
Intra-Peritoneal Administration	0th Day	0.0702	0.1731	0.0754	0.0624	0.0781	0.1731	0.0988	0.0802
		0.0667	0.1881	0.0584	0.0602	0.0914	0.1881	0.0882	0.0811
		0.0584	0.1984	0.0577	0.0544	0.091	0.1984	0.0732	0.0885
		0.0739	-	0.0564	0.0597	0.0862	-	0.0631	0.1068
		0.0593	-	0.0619	0.0571	0.0735	-	0.0694	0.0885
		-	-	0.0568	0.0699	-	-	0.0714	0.0784
	14th Day	0.1128	0.4483	0.0841	0.0608	0.1579	0.4483	0.1335	0.1769
		0.0649	0.6038	0.0761	0.053	0.1166	0.6038	0.1489	0.1353
		0.0756	0.6972	0.0599	0.0555	0.096	0.6972	0.1145	0.1771
		0.076	1.1227	0.0617	0.0547	0.1083	1.1227	0.1108	0.1553
		0.0734	0.6326	0.0672	0.083	0.1477	0.6326	0.1151	0.1314
		0.0626	-	0.0673	0.0481	0.1402	-	0.1451	0.1317
	28th Day	0.0627	0.3863	0.0542	0.0715	0.0745	0.3863	0.0984	0.1066
		0.0736	0.5717	0.0537	0.0772	0.091	0.5717	0.0935	0.1324
		0.0624	0.6917	0.082	0.0505	0.0876	0.6917	0.1226	0.1221

Table 12
Allergenicity profile i.e. specific IgE levels against rSt.HPV 16 and 18 expressing L1 proteins in mice.

Route of Administration	Euthanization Day	Anti-HPV 16 L1 IgE				Anti-HPV 18 IgE			
		Vehicle Control	OVA	1x HPV	5x HPV	Vehicle Control	OVA	1x HPV	5x HPV
Intra-Nasal Route	0th Day	0.0045	0.0045	0.0162	0.0050	0.0051	0.0048	0.0103	0.0047
		0.0104	0.0025	0.0014	0.0068	0.0080	0.0028	0.0018	0.0075
		0.0122	0.0017	0.0168	0.0123	0.0069	0.0020	0.0150	0.0060
		0.0147	0.0025	0.0040	0.0167	0.0091	0.0028	0.0026	0.0092
		0.0026	0.0026	0.0064	0.0129	-	0.0029	0.0039	0.0085
	28th Day	-	0.0033	0.0050	-	-	0.0036	-	-
		0.0057	-0.0001	0.0033	0.0033	0.0079	0.0002	0.0037	0.0004
		0.0032	-0.0012	-0.0004	-	0.0026	-0.0009	0.0002	0.0025
		0.0030	0.0023	0.0018	-	0.0047	0.0026	0.0021	0.0010
		-	-0.0009	0.0010	-	-	-0.0006	0.0013	-
	56th Day	-	0.0017	0.0013	-	-	0.0020	0.0015	-
		-	0.0010	0.0003	-	-	0.0013	-0.0008	-
		0.0047	-0.0002	0.0015	-0.0006	0.0052	-0.0001	0.0001	0.0024
		0.0026	-0.0004	0.0032	0.0035	0.0034	0.0014	0.0028	0.0021
		0.0029	0.0011	0.0017	-	0.0029	0.0020	-0.0012	-
	63rd Day	-	0.0017	0.0056	-	0.0012	0.0008	0.0014	-
		-	0.0005	0.0040	-	0.0024	0.0002	0.0069	-
		-	-0.0001	-	-	-	-0.0001	-	-
		0.0009	-0.0006	0.0010	-0.0001	0.0004	-0.0003	0.0588	0.0001
		0.0024	-0.0001	0.0014	0.0019	-0.0005	0.0002	-0.0006	0.0002
	73rd Day	0.0011	-0.0016	0.0016	0.0018	-0.0015	-0.0013	0.0005	-0.0003
		0.0012	0.0005	0.0026	-	-0.0017	0.0008	0.0020	-
		-	0.0000	-	-	-	0.0003	-0.0015	-
		-	0.0009	-	-	-	0.0012	0.0025	-
		0.0061	0.0000	0.0225	0.0003	0.0001	0.0003	0.0004	0.0018
	-0.0018	0.0004	-0.0005	-0.0005	-0.0004	0.0007	-0.0033	0.0019	
	-	-0.0008	-	-	-	-0.0005	-	-	

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Table 12 (continued)

Route of Administration	Euthanization Day	Anti-HPV 16 L1 IgE				Anti-HPV 18 IgE			
		Vehicle Control	OVA	1x HPV	5x HPV	Vehicle Control	OVA	1x HPV	5x HPV
Intra-Peritoneal Administration	0th Day	0.1531	0.1504	0.1227	0.1535	0.1729	0.1504	0.1522	0.1777
		0.1718	0.1471	0.122	0.1623	0.2098	0.1471	0.1484	0.1666
	14th Day	-	0.1699	-	-	-	0.1699	-	-
		0.1793	0.2897	0.1709	0.2089	0.1959	0.2897	0.1785	0.2258
		0.2194	0.4485	0.1842	0.1997	0.2637	0.4485	0.1849	0.2206
		-	0.5106	-	-	-	0.5106	-	-
		-	0.4622	-	-	-	0.4622	-	-
		-	0.3672	-	-	-	0.3672	-	-
	28th Day	0.1759	0.2589	0.1711	0.1901	0.1871	0.2589	0.1497	0.2021
		0.2141	0.3641	0.1645	0.1768	0.1418	0.3641	0.1481	0.1908
		-	0.3954	-	-	-	0.3954	-	-

Ethics Statement

The test compound of current article is genetically engineered *S. typhi* Ty21a vector comprising of HPV 16 and 18 L1 protein coding genes; hence the sub-chronic testing was undertaken after obtaining the approvals from Institutional Bio-safety Committee (IBSC) and Review Committee on Genetic Manipulation (RCGM- DBT, India) [4]. In addition, the study design and experimental procedures followed for sub-chronic testing of recombinant HPV vaccine were approved by the Institutional Animal Ethics Committee (IAEC) (IAEC/Proj/08/21,012,008) of ICMR-National Institute of Nutrition, Hyderabad, India.

CRediT Author Statement

Srinivasa Reddy Y.: Experimental execution and data compilation along with manuscript preparation and communication; **Narendra Babu K.:** Immunological and allergenicity profile execution, compilation and interpretation; **Uday Kumar P.:** Supervision of haematological and histopathological examination; **Qadri S.S.Y.H.:** Animal health monitoring and interpretation of test compound effect, if any during the course of experiment; **Surekha M.V.:** Analysis and interpretation of haematological and histopathological data; **Dinesh Kumar B.:** Study design, supervision, and study-director.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships which have, or could be perceived to have, influenced the work reported in this article.

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