Safety & Immunogenicity/ Seroconversion Results Using Needle Free Injection Systems

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Summary of Immunogenicity/ Seroconversion Results from Clinical Trials/Literature Studies

Safety, Tolerability and Immunogenicity / Seroconversion results from clinical trials / literature studies conducted using Needle Free Injection System.

1. **Safety, Tolerability and Acceptability Study of Needle-Free Injection System Vs. Conventional Hypodermic Needle, India**
   - Saline was administered to approximately 60 volunteers.
   - IntegriMedical's Needle Free Injection System (NFIS) is safe, tolerable & acceptable.
   - No significant difference in terms of tenderness, redness, induration, vital & systemic examination parameters.
   - Following is the table comparing Vas Score for Needle-Free injection and Convention Hypodermic Needle Injections.

Pain Score (Vas Score)		**NF Injection (N=30)**	**CHN Injection (N=30)**
		No. (%) of Subjects	
None	(0)	77%	30.0%
Mild	(1,2, or 3)	23%	70.0%
Moderate	(4,5, or 6)	0.0%	0.0%
Severe	(7,8,9, or 10)	0.0%	0.0%

2. **Immunogenicity & Safety Study, India**
   - Covid Vaccine (Covishield)
   - Vaccine was administered in adults and children using the needle-free injection system for approximately 220 volunteers. The immunogenicity levels using the needle free injection was at par or better than the conventional hypodermic needle.
   - The safety, acceptability and tolerability were observed in children and 47% children experienced zero pain using the needle free injections
   - Following is the table comparing the immunogenicity levels –

Table 4: Summary statistics of concentration of IgG, IgA, and IgM

Immunological Parameters		**Group T1 (N=71)**			**Group T2 (NFIS) (N=67)**		
		Pre Dose	**Post Dose**	**P-value (paired t-test)**	**Pre Dose**	**Post Dose**	**P-value (paired t-test)**
IgG concen.	Mean	1083.32	1296.77	0.000	1107.93	1306.75	0.000
	STDEV	174.86	198.32		211.61	197.35	
IgA concen.	Mean	193.24	304.08	0.000	188.88	282.95	0.000
	STDEV	64.32	66.74		63.11	77.02	
IgM concen.	Mean	119.80	197.01	0.000	124.24	189.37	0.000
	STDEV	50.32	55.42		57.10	49.24	

*** Group T1 - Hypodermic Needle,
Group T2 – Needle Free Injection System

3. **Immunogenicity & Safety Study, India (Bavdekar 2018) –**
   - MMR Vaccine
   - Randomized, parallel group, non-inferiority trial
   - Multicentric clinical study was conducted for administration of MMR vaccine in India using needle-free injections and conventional needle syringe (N-S). MMR Vaccine was administered subcutaneously in the anterolateral aspect of the thigh region.
   - On evaluation of the immunogenicity results, it was observed that at baseline, seropositivity rates were similar between both the groups for all three antigens. On day 35, seropositivity rates in the DSJI and N-S groups were 97.5% and 98.7% for measles; 98.8% and 98.7% for mumps; and 98.8% and 100% for rubella.
   - Similar studies were conducted in Brazil on 582 volunteers (de Menezes Martins Reinaldo 2015)

4. **Immunogenicity and Tolerance Study, France & Africa (Isabelle Parent du Chfitelet 1997)**
   - DTP Vaccine
   - Vaccine was delivered by needle-free injection and compared with standard syringe injection to infants and immunogenicity results are as follows –

Type of Antigen	Diphtheria		Tetanus		Pertussis	
	Imule (Needle Free)	Syringe	Imule (Needle Free)	Syringe	Imule (Needle Free)	Syringe
Pre-vaccinal GMT (IU ml-')	0.05 (0.04-0.68)	0.07 (0.06-0.08)	0.09 (0.07-0.12)	0.17 (0.12-0.23)	10.6 (7.6-14.5)	9.7 (7.1-13.3)
Post-vaccinal GMT (IU ml-')	0.55 (0.44-0.69)	0.34 (0.27-0.41)	2.27 (2.12-2.43)	1.46 (1.29-l .65)	1434 (1188-l 732)	1188 (965-l 465)
Seroconversion %	79.2%	56.7%	88.7%	70.3%	94.4%	94.6%

*GMT = Geometric Mean Titter

   - Similar study was conducted on Pentavalent diphtheria, tetanus, pertussis (whole cell), hepatitis B (rDNA), and Haemophilus influenzae type b conjugate vaccine administered with needle-free injections. Seropositivity rates for the DSJI and N-S groups in the per-protocol population at baseline and at day 84 post vaccination appeared comparable, by descriptive statistics, for all vaccine components.
   - Table below provides Seroprotection/Seropositivity at days 0 and 84 after vaccination
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Vaccine component	Day 0		Day 84	
	Disposable-syringe jet injector (n = 61)	Needle and syringe (n = 67)	Disposable-syringe jet injector (n = 61)	Needle and syringe (n = 67)
Diphtheria	4 (6.6%)	7 (10.4%)	61 (100.0%)	64 (95.5%)
Tetanus	61 (100.0%)	66 (98.5%)	61 (100.0%)	66 (98.5%)
Pertussis	3 (4.9%)	1 (1.5%)	36 (59.0%)	41 (61.2%)
Hepatitis B	9 (14.8%)	9 (13.4%)	60 (98.4%)	66 (98.5%)
Haemophilus influenzae type B (long- term protection)	21 (34.4%)	24 (35.8%)	56 (91.8%)	62 (92.5%)
Haemophilus influenzae type B				