INCUBATION CENTRE AT SVSIDS

Report On Activities and Achievements From 2013-2019

The institute is a post-graduate dental school attached to a medical college and a full-service preclinical research centre capable of toxicology, product assessments, initial product development and exploratory small and large-mammal studies. In 2012, an 'Incubation Centre & Intellectual Property Cell', adhering initially to self-developed guidelines and later amended to conform to the National Intellectual Property Rights Policies, 2016 & 2019, was instituted. Standard operating procedures (SOPs) for conducting clinical trials with a view to promote commercialization in affiliated institutions were developed. Some of the guidelines pertinent to this report were as follows; 1. Within ethical guidelines, novel products, materials or devices developed 'in-house' or procured from a source with no commercial interests must be given

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precedence in clinical trials. 2. Pre-clinical testing such as biocompatibility assays should be performed within the institution whenever possible. 3. For all clinical trials, primary outcomes, which are the variables most relevant to answer the research question must be clearly defined and 4. Data on financial and human resource aspects of clinical trials must be collected from the beginning to the end of a trial in a specified format. All studies from 2013/14 onwards adhered to these guidelines.

Profile and Growth of R & D projects

In the initial stage, 440 clinical trials (258 dissertations and 182 independent studies) done between 2014-19 in the institution were analyzed. Institutional or self-financed phase II trials on human subjects meeting regulatory standards for ethical research and evaluating novel products, tests or devices with at least two primary outcomes were included in the analysis. Animal studies, *in vitro* investigations and trials on established and commercially available products were excluded.

The primary purpose of every clinical trial was identified and based on its similarity with other trials investigating similar generic products, tests or devices, they were grouped together into 'projects' under the following headings: Irrigants, diagnostic devices, surgical devices, biomaterials and gels. 338 clinical trials were grouped into 188 projects under the above headings and the trials required *per* project, money spent (capital/trial), material cost/trial (in ₹), skilled labour/trial and the cycle time/trial were calculated. Each project yielded a product. Variables in the project were defined as follows; 1. Material cost/trial[⁋]= Production cost+ delivery charges + warranty charges + special equipment charges 2. Cycle time[‡]= time from the beginning to the end of the trial. 3. [⁂]Labour= a single primary investigator with any number of sub-investigator (or) research assistant. 4. Capital/trial= [Study Costs (Material cost/trail[⁋] + (administrative staff costs*cycle time[‡])) + Patient Costs ((procedure cost*subjects)

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+ ((paramedical staff charges + assistant researcher charges) *cycle time‡) + (biospecimen processing charges*subjects)) + Labour charges (‡Labour*cycle time‡)]. The compounded growth rate (CGR) per year was calculated for 5 years to identify the trend in the number of projects/products fit for commercialization. The CGR (in %) was calculated as follows; $CGR=[(P_{final}/P_{begin})^{1/t}-1] *100$ where P_{begin} and P_{final} are the number of products at the beginning and end of the year of the year and 't' is time in years.

DATA ANALYSIS

Profile and Growth of R & D projects

338 institutional or self-financed trials from 2014 to 2019 on human subjects evaluating novel products, tests or devices (phase II) were grouped into 188 projects. *Table I* summarizes the distribution of variables such as P_k-values, number of projects, trials per project, capital, material cost, labour and cycle time under the headings: Irrigants, diagnostic devices, surgical devices, biomaterials and gels. A significant to highly significant distribution *(p=0.001)* was seen for number of projects, P_k scores *(p=0.02)*, trials per project *(p=0.04)*, capital and material costs across the headings. Surgical devices had least number of projects (4 out of 188); however, this category also had the highest numbers for all the other variables. The opposite was observed for projects under irrigants. Highest P_k score was observed for projects in diagnostic devices group. CGR per year for projects was not constant; rather there were yearly variations. From 2014-19 (79 projects) to 2018-19 (188 projects), the CGR growth over five years was 19.23% per year.

Identification of projects with the potential for commercialization

Probability of k-success events in Bernoulli trials was calculated for all trials and individual trails to determine whether a product is suitable for commercialization or not. $X_1 \geq 0.15$ was the chosen cut-off value to identify products with potential for commercialization.

The initial pool of 188 research projects narrowed down to 22 commercialization-focussed projects with 59 trials in total. *Table II* summarizes the distribution of variables such as P_1-values, number of projects, trials per project, capital, material cost, labour and cycle time under project headings. A trend similar to previous observations made before the cut-off was seen. Previously insignificant, a significant distribution *(p=0.0126)* was seen for labour/trial across all projects. Higher number of projects were seen for biomaterial and irrigant groups.

Table III summarizes the comparison of all variables before and after the identification of commercialization-worthy projects through the application of cut-off of probability of success scores. The measures for labour and cycle time remained unaffected *(p>0.05)*. Trials/project for irrigants *(p=0.1)* and surgical devices *(p=0.09)* did not show significant differences as well. P_k vs P_1 values for gels remain unaffected. The remaining variables showed significant to highly significant differences across all projects.

Identification of products for actual commercialization

Projects with $X_2 \geq 0.20$, were assumed as having products with potential for actual commercialization. Three products were identified as having a potential for commercialization. They are 1. A low-cost oral cancer detection device *(Product 1)* 2. A butyrate inactivated recombinant human bone morphogenetic protein-2 *(rhBMP-2)* gel for bone regeneration *(Product 2)*. 3. basic fibroblast growth factor (bFGF) impregnated collagen membranes for soft-tissue regeneration *(Product 3) (Figure I)*. *Table IV* summarizes the products identified for commercialization and the variables under them. Total project cost was higher for product-3 whereas material costs were higher for product-2. Both the products also had more trials per project (4/project). Cycle time, labour required and subjects under the project were maximum for product-1.

Determinants of Commercialization

On comparing hypotheses with their associated variables, it appears that greater number of trials ($\chi 2=4.6793$; $p=0.030528$) and successes ($\chi 2=20.8134$; $p<0.00001$) in a project along with a higher capital ($\chi 2=12.2662$; $p=0.000461$) will generate a product worthy of commercialization. The number of investigators/trial and the trial duration seem to have no effect on the outcomes of a commercialization *(Table V)*.

SUMMARY

To conclude, we had analyzed research projects done in our institution within the last five-years to identify products or devices with the potential for commercialization and sought to understand the effect of product-development variables to define future strategies to improve quality of clinical trials in commercialization-oriented projects. Product development and commercialization are money-driven and as in any form or research, capital plays an important role in sustaining clinical trials. At the same time, greater number of trials and successes of those trials were significantly associated with products worthy of commercialization. A steady increase in projects and trials is an essential part of product development and commercialization and a 10% CGR over the five-year period is an indicator of healthy growth in commercialization-worthy projects. However, the number of investigators (labour) per trial and the trial duration seem to have no effect on the outcomes of a commercialization. Three products were identified and commercialization of these products is being actively pursued and one of the devices has already been patented. The results seem to suggest that in trials for commercialization, emphasis must be placed on implementing multiple well-designed clinical trials on a device or product to successfully identify whether it is commercialization-worthy or

not. Due attention must be given to the financial aspects of the projects as deficiencies may result in negative impact on the flow and outcomes of a clinical trial.

REPORT SUMMARY

One of the first steps in commercialization of a product is the identification and selection of new products and/or ideas. In an academic institution which generates a lot of multi-disciplinary data, it can be a daunting task. Clinical data is the only record an investigator has access to, and from this, various commercialization worthy ideas or concepts can be identified or generated. The quality of a commercialization-worthy idea or a product is highly dependent on factors such as the quality of clinical data, capital, materials cost and skilled labour involved in the project. In dentistry at least, there seems to be a paucity of literature regarding identification of commercialization-fit products from various clinical trials and the effect of variables such as capital, material cost, labour and time on commercialization-oriented projects. In this context, we sought to analyse research projects done in our institution to identify products or devices with a potential for commercialization and understand the effect of product-development variables such as number of trials, capital, material costs, labour and time on clinical trials for defining future strategies for turning ideas and products into commercialization-worthy products.

Product development and commercialization are money-driven and as in any form or research, capital plays an important role in sustaining clinical trials. At the same time, greater number of trials and successes of those trials were significantly associated with products worthy of commercialization. A steady increase in projects and trials is an essential part of product development and commercialization and a 10% CGR over the five-year period is an indicator of healthy growth in commercialization-worthy projects. However, the number of investigators (labour) per trial and the trial duration seem to have no effect on the outcomes of a commercialization. emphasis must be placed on implementing multiple, well-designed clinical trials on a device or product to successfully identify whether it is commercialization-

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worthy or not. Due attention must be given to the financial aspects of the projects as deficiencies may result in negative impact on the flow and outcomes of a clinical trial

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IMPLICATIONS OF OUTCOMES FOR VARIOUS STAKEHOLDERS IN THE MANAGEMENT

We had analyzed research projects done in our institution within the last five-years to identify products or devices with the potential for commercialization and sought to understand the effect of product-development variables to define future strategies to improve quality of clinical trials in commercialization-oriented projects. Three products were identified and commercialization of these products is being actively pursued and one of the devices has already been patented. An entrepreneur should have a thorough understanding of the effect of product-development variables such as number of trials, capital, material costs, labour and time on clinical trials for defining future strategies to improve quality of research projects in commercialization-oriented projects.

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ANNEXURES

TABLES

Table I: Products identified from 188 projects (338 clinical trials; 2014-19) and the distribution of variables under them.

Products	No. of Projects	P_k /Project	Trials per project	Capital/trial (₹)	Material Cost (₹)/trial	Average Labour /trial	Cycle time/trial (Months)
Irrigants	92	0.13±0.07	1.08±0.19	2,19,405±1,20,005	26,038±20,831	3±2	9±1.2
Diagnostic devices	12	0.17±0.12	1.66±0.70	11,84,806±1,72,083	4,96,474±2,27,179	7±3	14±3.8
Surgical devices	4	0.16±0.09	6.25±1.25	22,68,778±9,25,021	5,80,327±2,76,087	11±6	16±5.2
Biomaterials	36	0.15±0.08	3.33±1.65	7,01,464±2,84,389	29,359±22,491	3±2	11±4.0
Gels	44	0.14±0.04	1.70±0.82	3,64,770±1,57,818	73,965±34,416	3±1	9±4.1
F-Value ***p value***	62.81 0.001**	6.32 0.02*	66.92 0.04*	143.78 0.001**	98.21 0.001**	1.56 0.34‡	17.23 0.20‡

P_k =k successes in n trials ‡Non-significant *Significant **Highly significant

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Table II: Identification of projects identified as having a potential for commercialization after applying the cut-off ($X_1 \geq 0.15$; 22 projects, 59 trials).

Products	Number	P_1 /Project	Trials/ Project	Capital/ trial (₹)	Material Cost// trial (₹)	Labour/trial (individuals)	Cycle time/ trial (Months)
Irrigants	*8*	0.17±0.04	1.21±0.01	3,53,147±28,680	40,756±9,358	4±1	9±0.8
Diagnostic devices	*1*	0.24±0.06	2.01±0.24	13,75,984±3,86,960	7,41,089±1,58,195	8±2	16±3.2
Surgical devices	*1*	0.19±0.07	7.29±0.22	26,40,643±4,82,285	7,93,393±1,43,176	13±4	18±4.3
Biomaterials	*9*	0.20±0.04	4.22±0.69	9,12,794±97,136	93,794±18,902	4±2	12±2.7
Gels	*3*	0.15±0.01	2.02±0.41	4,92,097±39,247	1,16,910±17,510	3±1	10±3.4
F-Value	6.98	1.22	23.81	66.92	67.82	6.43	1.53
p value	0.01*	0.012*	0.02*	0.04*	0.00011**	0.0126*	0.2282‡

P_1 =k successes in n trials ‡Non-significant *Significant **Highly significant

Table III: Comparison of all variables before and after the identification of commercialization-worthy projects through the application of X_1 cut-off of probability of success scores.

Type of the products	Number of projects	P_k vs P_1 /Project	Trials/ Project	Capital/ trial (₹)	Material Cost/ trial (₹)	Labour/trial (individuals)	Cycle time/ trial (Months)
Irrigants	≤0.001**	≤0.001**	0.1‡	≤0.001**	≤0.001**	0.09‡	0.7‡
Diagnostic devices	≤0.001**	≤0.001**	0.003*	0.03*	0.05*	0.07‡	0.09‡
Surgical devices	≤0.001**	≤0.001**	0.09‡	0.004*	≤0.001**	0.06‡	0.07‡
Biomaterials	≤0.001**	≤0.001**	0.04*	≤0.001**	≤0.001**	0.3‡	0.1‡
Gels	≤0.001**	0.2‡	0.05*	≤0.001**	≤0.001**	0.1‡	0.09‡

P_k & P_1 =k successes in n trials ‡Non-significant *Significant **Highly significant

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Table IV: Products identified for final commercialization and the distribution of variables under them ($X_2 \geq 0.20$).

Products	P_2	Trials/ Project	Subjects	Total Cost (₹)	Material Cost (₹)	Total Labour (individuals)	Cycle time (Months)
Oral cancer detection device	0.28	2	187 (3)	40,54,743 (1,93,439)	14,47,459 (1,92,774)	15 (1)	18 (2)
RhBMP-2 gel	0.23	4	118 (2)	42,63,356 (1,57,063)	19,06,649 (1,19,401)	14 (2)	13 (2)
bFGF impregnated collagen membranes	0.23	4	97 (3)	44,50,534 (1,49,968)	15,93,025 (1,73,441)	15 (1)	14 (2)

[a)] Reported numbers represent weighted averages and SD (in parenthesis) of five observations rounded off to the nearest integer. P_2 =k successes in n trials.

Table V: Comparison of hypotheses with their associated variables; H1: Greater number of trials H2: Greater successes (k) in clinical trials H3: Higher capital H4: Higher man-force and H5: A higher cycle-time

Hypothesis *vs* Variables	$\chi 2$	p=value
H1 *vs* >1 trial/project	4.6793	0.030528*
H2 *vs* >2 successes/project	20.8134	<0.00001**
H3 *vs* > 3,00,000 ₹/trial	12.2662	0.000461**
H4 *vs* >4 individuals /trial	3.068	0.079848‡
H5 *vs* >12 months/trial	3.4254	0.064199‡

$\chi 2$= chi-square statistic ‡Non-significant *Significant **Highly significant

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FIGURES

Figure I: Three products were identified as having a potential for commercialization. They are 1. A low-cost oral cancer detection device *(left)* 2. A butyrate inactivated recombinant human bone morphogenetic protein-2 (rhBMP-2) gel for bone regeneration *(middle)* and 3. basic fibroblast growth factor (bFGF) impregnated collagen membranes for soft-tissue regeneration *(right).*

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