

PROJECT PROFILE

CLINICAL RESEARCH TRAILS (I, II & III)

PREPARED BY



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1.1 INTRODUCTION

Objective

The main aim is to development of knowledge based, high value added services to the pharmaceutical industry. This is to be achieved through offering contract research and manufacturing services (CRAMS).

Activities:

India having demand from prospective clients like Johnson & Johnson, Pfizer, GlaxoSmithKline, Roche, Sanofi-Aventis, Novartis, AstraZeneca, Abbott Laboratories, Merck, Wyeth, Bristol-Myers Squibb and Eli Lilly to provide Clinical Trails in Phases of (I, II & III), Preclinical trails and Manufacturing support for the formulations developed at the center. This will provide the client a manufacturing base in the initial years of market development. And also R&D support and manufacturing back up under one roof will be more attractive to clients and would be a good source of revenue.

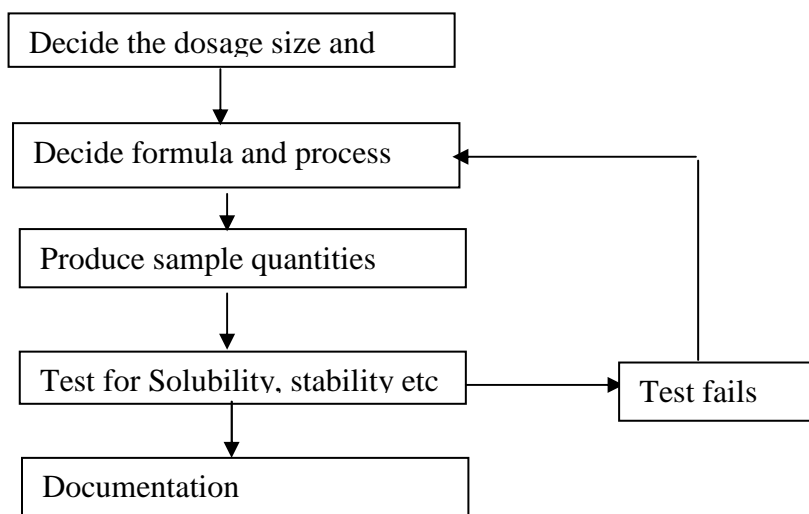
1.2 TECHNOLOGY AND PROCESS

The profile will be providing complete services for formulation development and support the client with manufacturing service during the initial years

The products for which services are provided cover New chemical entities (NCE's), generics, specialty products, reformulation and life cycle extension of existing molecules

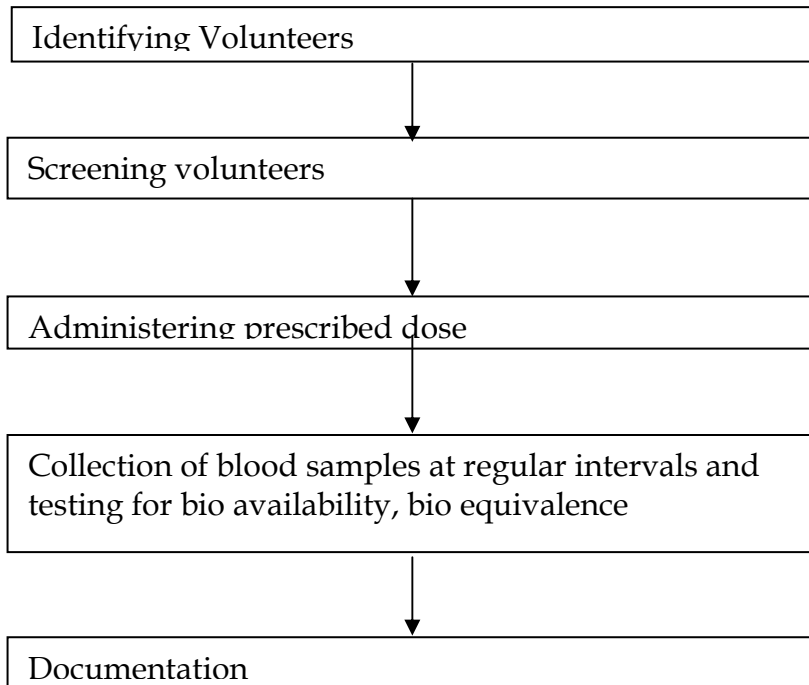
FORMULATION DEVELOPMENT

The first stage is development of suitable dosage form. In case of generics the client usually specifies the dosage form and size. The formulation development process goes through the following steps.



CLINICAL TESTING

The formulation developed is to undergo clinical testing before regulators approve it. Clinical testing (phase I) involves the following steps



FORMULATION MANUFACTURING

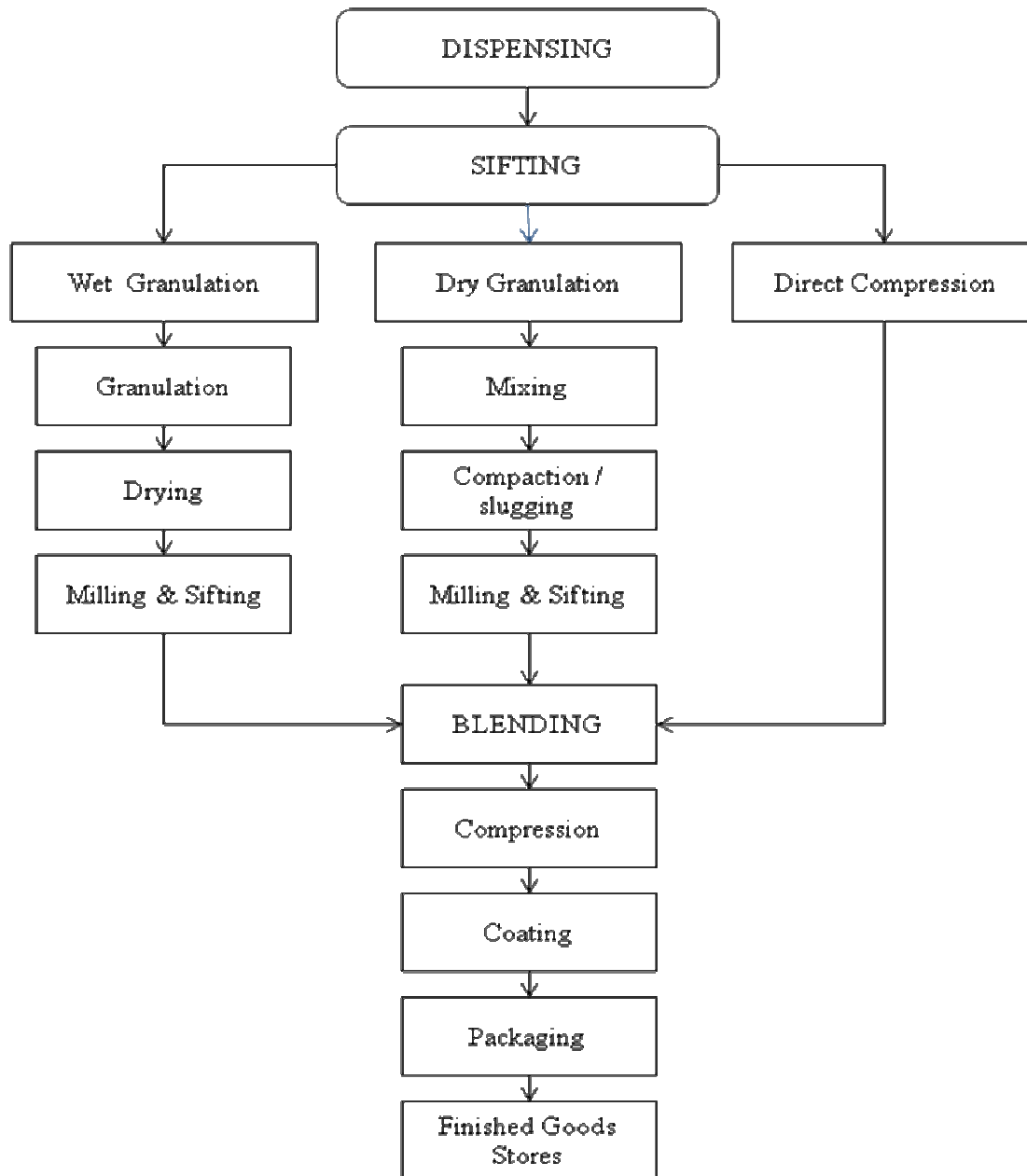
For manufacturing activity will concentrate on two Categories

- Tablets
- Capsules

Tablets:

The process flows through the following steps.

Manufacturing Flow chart for Tablets

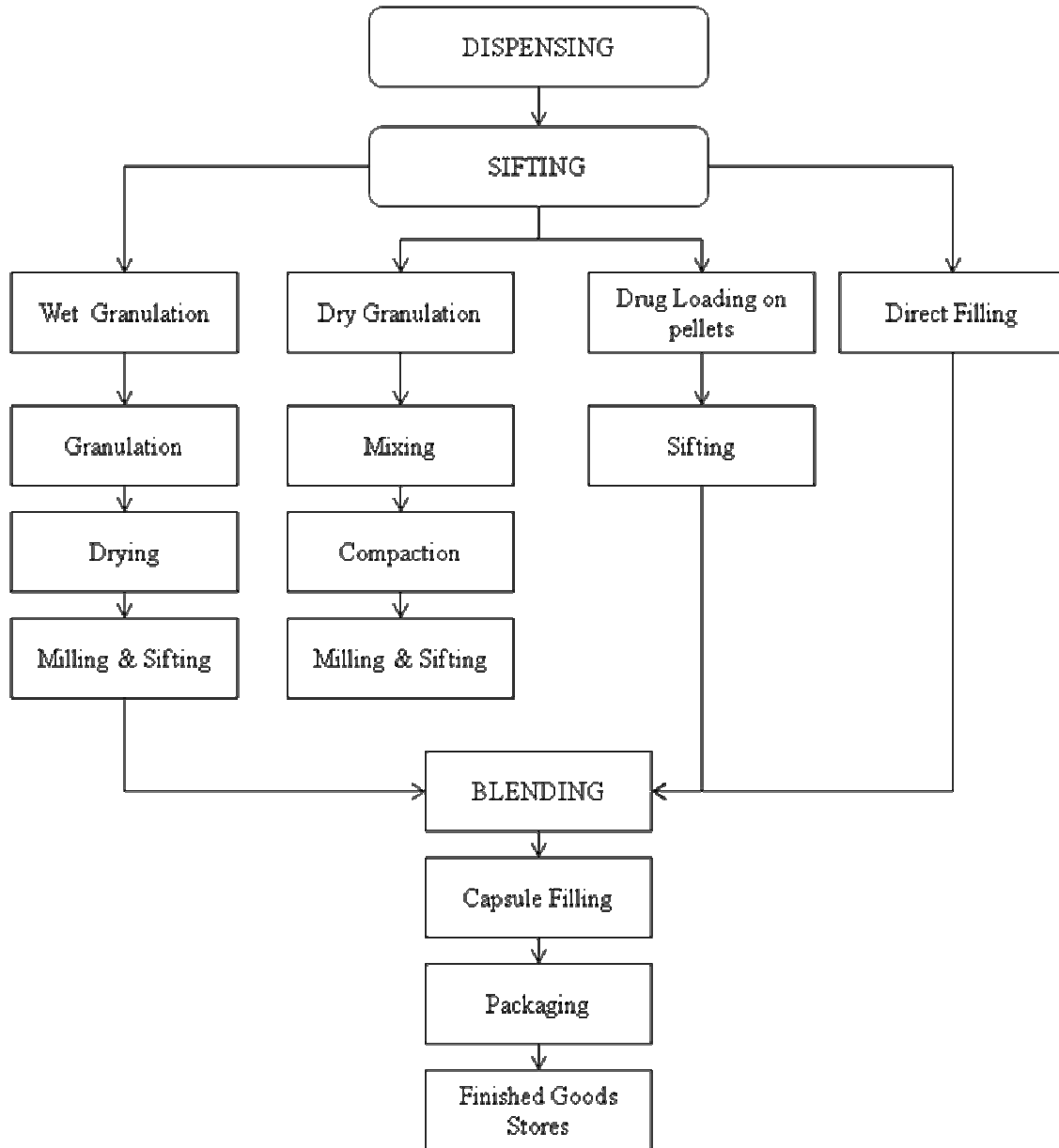


QUALITY CHECKS ARE CARRIED OUT AT DIFFERENT STAGES AS DEFINED BY THE CLIENT

Capsules:

The process flows through the following steps.

Manufacturing flow chart for Capsules

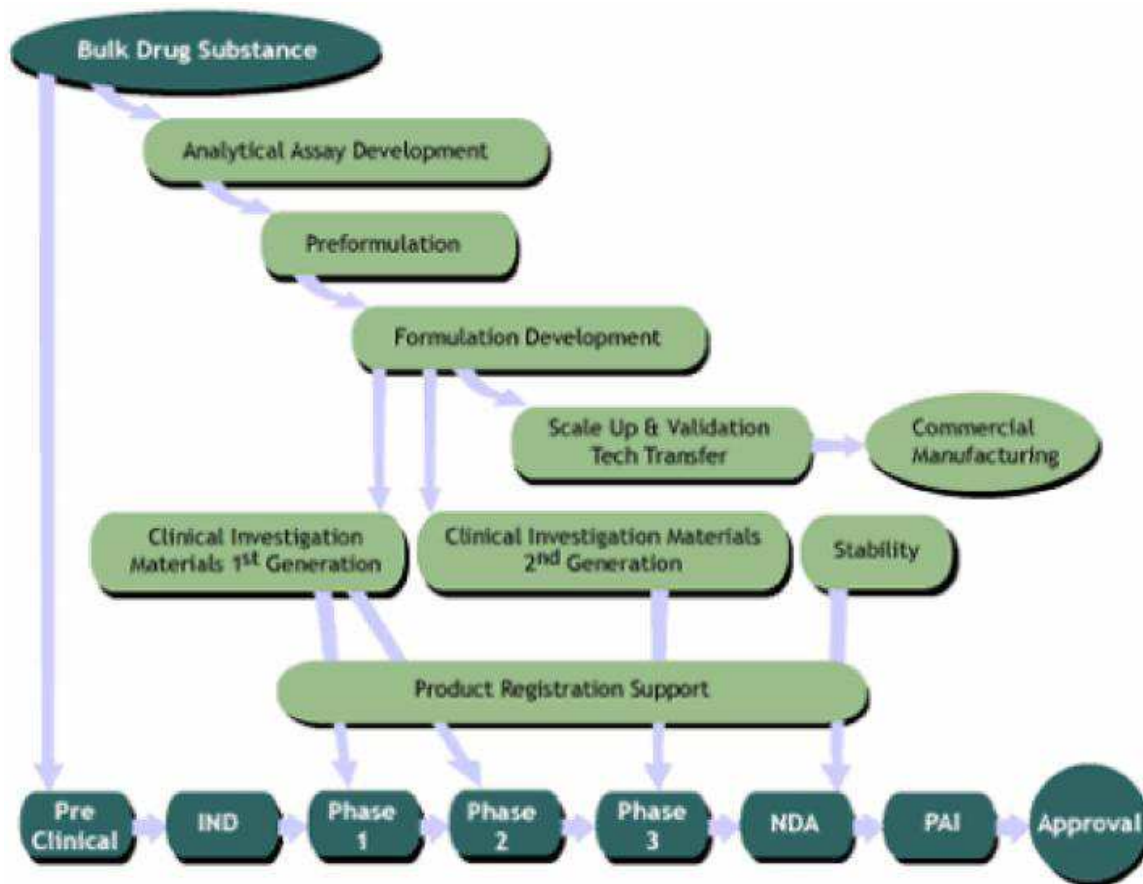


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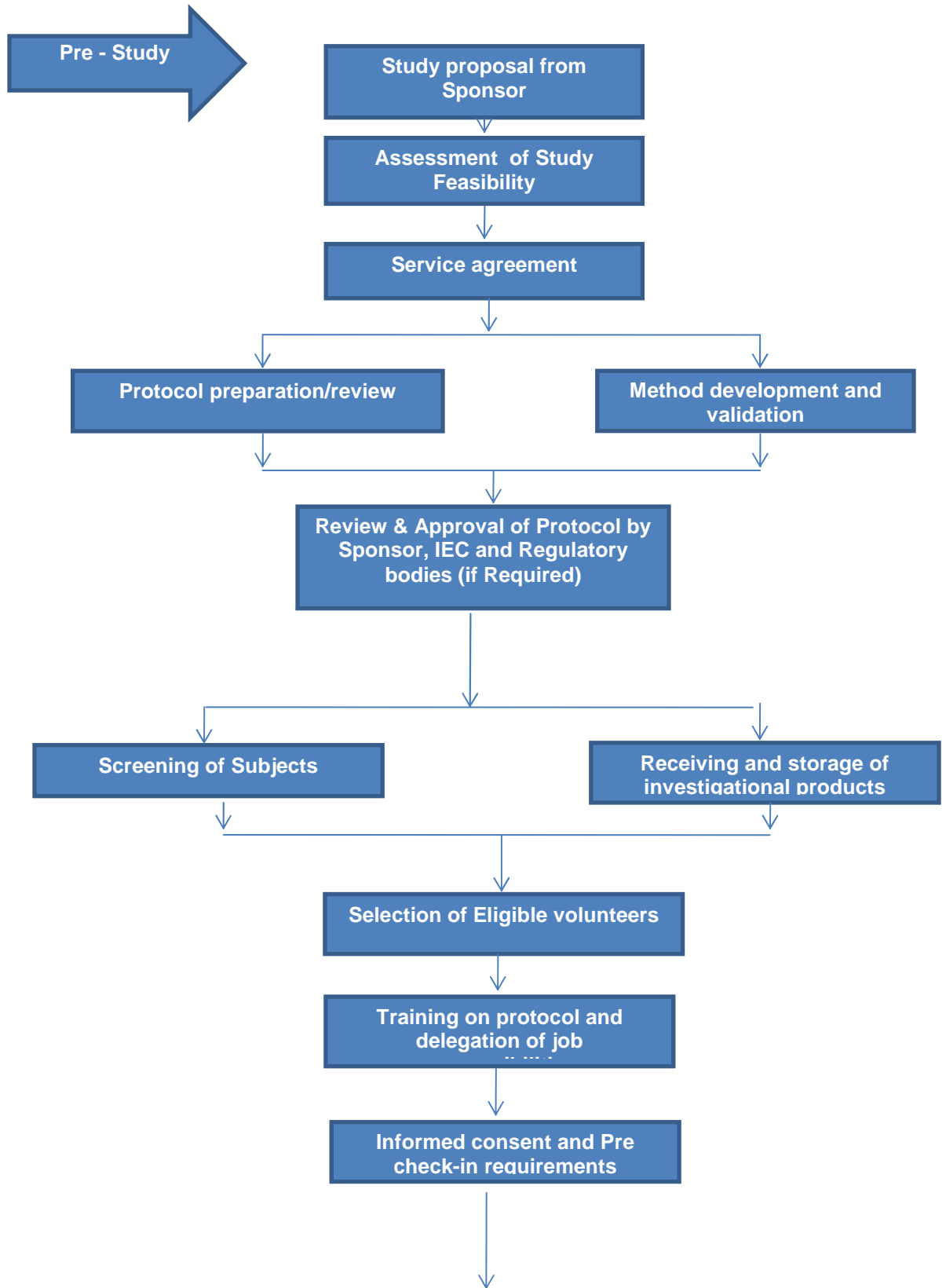
Technology availability and development work:

Technology will be the main strength, which is nothing as simple as the core team comprising of highly experienced Technologists with chemistry and Pharmacy background.

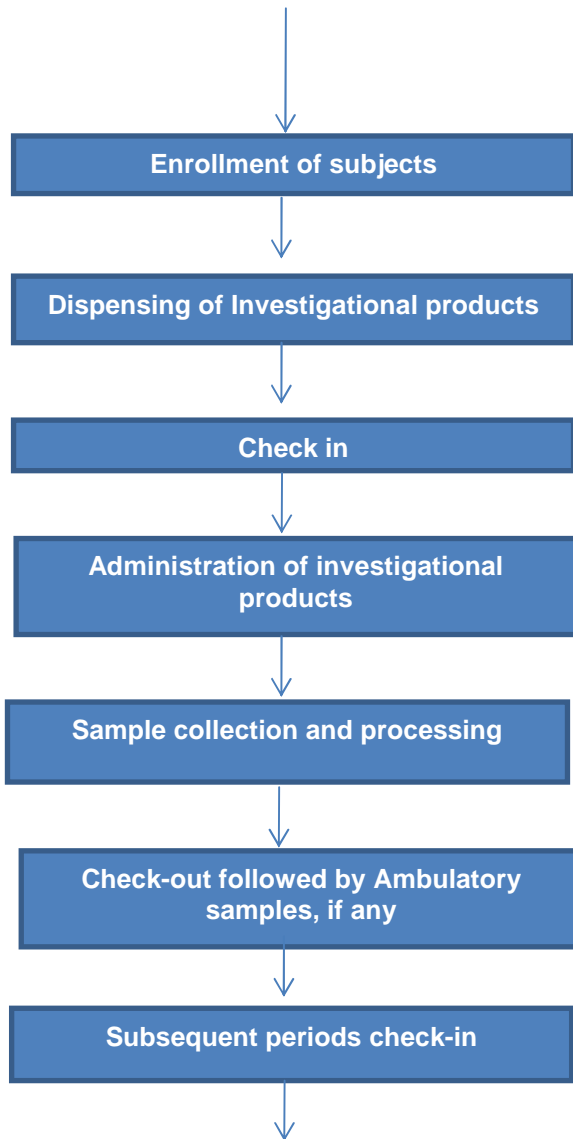
Business Process Flow

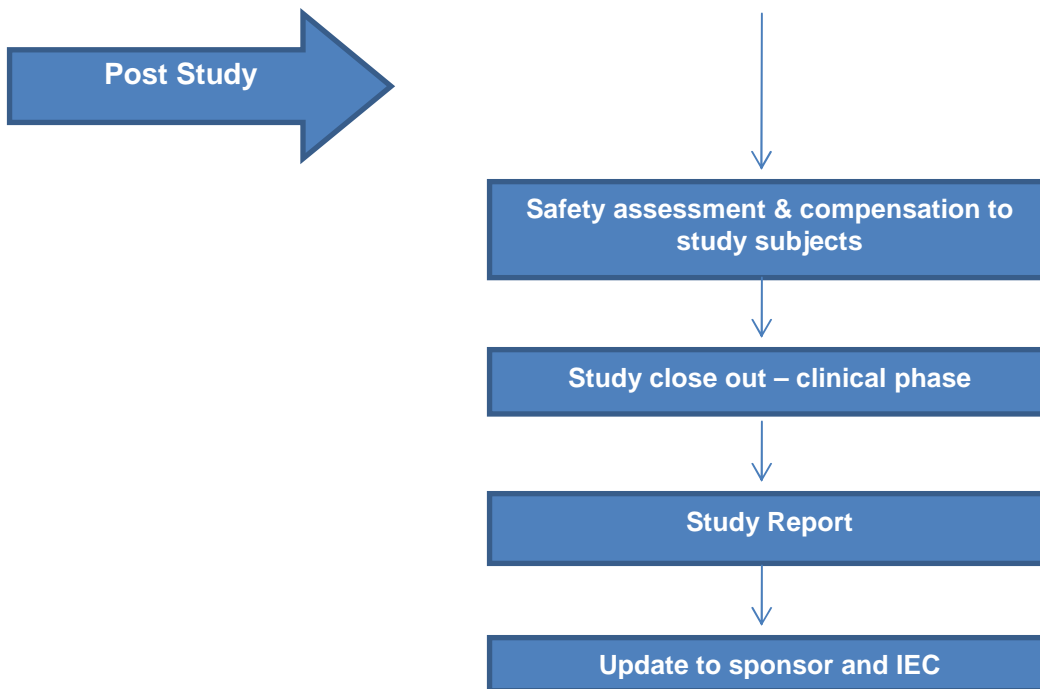


FLOW OF ACTIVITIES IN CLINICAL STUDIES



During Study





1.3 ADVANTAGES OF CLINICAL TRAILS & SUPPORT MANUFACTURING PLANT

India as the preferred destination for CRAMS...

India offers distinct economic advantages to large pharmaceutical companies who are looking to reduce their time-to-market on new products and save at the same time. These include:

- Strong development skills as demonstrated in the international market – APIs and dosage forms
- Low R&D cost
- Cost of manufacturing is 40-50 per cent lower as compared to western countries
- Integrated business model creating a one-stop shop for innovators
- India has six times the number of trained chemists as compared with the US
- With over 80 USFDA approved plants, India has the highest number of FDA approved plants outside the US
- Abundant English speaking skilled manpower
- Large patient population providing a diverse pool for clinical trials for NCEs
- High quality telecom and IT infrastructure
- Most importantly, Indian companies have adapted to international regulatory norms & respect IPR

1.4. APPLICATIONS

CRAMS could cover **New chemical entities (NCE)** or **generics**.

NCE ARE NEW PRODUCTS IDENTIFIED AND PATENTED BY AN INVENTOR COMPANY. BEFORE GETTING THE APPROVALS TO MARKET THE DRUG FROM REGULATORY AGENCIES LIKE US FDA, THE INVENTOR COMPANY HAS TO CARRY OUT PRECLINICAL (ON ANIMALS) AND CLINICAL (ON HUMAN VOLUNTEERS) TESTING FOR TOXICITY AND EFFECTIVENESS, DEVELOP SUITABLE DOSAGE FORMS, AND TEST THE DOSAGE FORMS FOR STABILITY ON STORAGE AND A HOST OF OTHER CHARACTERISTICS. THE INVENTOR HAS TO FILE THE DETAILS IN NEW DRUG APPLICATION (NDA) THE REGULATORY AUTHORITIES APPROVAL WILL DEPEND ON THEIR BEING SATISFIED WITH THE RESULTS.

GENERICS ARE PRODUCTS THAT ARE OFF PATENT DRUGS THAT ARE PRODUCED BY COMPANIES OTHER THAN THE INVENTOR COMPANY. THESE COMPANIES MAY INTRODUCE THE PRODUCT IN A DIFFERENT DOSAGE (SAY DOUBLE STRENGTH) OR GO FOR A NEW / NOVEL DRUG DELIVERY SYSTEM (NDDS) LIKE SLOW RELEASE DOSE OR JUST COPY THE INVENTOR. IN REGULATED MARKETS LIKE USA THE GENERIC MANUFACTURER HAS TO FILE AN ABBREVIATED NEW DRUG APPLICATION (ANDA) CONTAINING COMPARATIVES STUDIES WITH THE ORIGINAL PRODUCT. THIS INVOLVES ANALYTICAL AND CLINICAL RESEARCH. GENERIC MANUFACTURERS START THE WORK TWO OR THREE YEARS BEFORE THE PATENT IS TO EXPIRE AND COLLECT ALL THE REQUIRED INFORMATION. THE INVENTOR COMPANIES AND THE GENERIC MANUFACTURERS MAY OUTSOURCE SOME OF THE WORK FROM A CRAM SERVICE PROVIDER.

In the developed countries there a number of small companies providing CRAM services to the big pharma companies.

1.5. MARKET

The market drives more on Formulation Development, Clinical Research Services. Manufacturing services will be used to provide support to clients in marketing the formulations developed.

Contract research & manufacturing services (CRAMS) is a fast growing segment of the pharmaceutical industry in India. As the title indicates CRAMS deals with manufacturing and research activities carried out by the service provider company under a contract to the service buyer company

In the pharmaceutical industry CRAMS cover

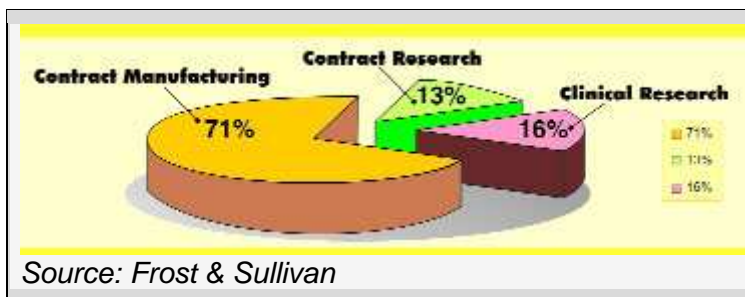
Contract Research

Clinical Research

Contract Manufacturing

As per one report (Cygnus research) the global pharmaceutical outsourcing market was worth USD57.2 billion in 2007. It is expected to grow at a CAGR of 10% to reach USD76 billion by 2010. Global market for Contract Research and Manufacturing Services (CRAMS) in 2007 is estimated to be USD55.48 billion. Out of the total global CRAMS market, contract research was USD16.58 billion, growing at a CAGR of 13.8% and

contract manufacturing was USD38.89 billion accounting for the major share (approximately 68%) of the total global pharmaceutical outsourcing market.



The work covered by the three branches

Contract manufacturing	Contract research	Clinical research
Manufacture of formulations	Product development	Pre clinical trials
Manufacture of Active Pharmaceutical Ingredients (API) / Manufacture of Intermediates (custom synthesis)	Process development Analytical research	Clinical trials

Over the last five years the CRAMS industry has been contributing close to eight percent of the Indian pharma business. India, with more than 100 US FDA-approved manufacturing facilities, is one of the most preferred locations for outsourcing manufacturing services in India by the multinationals and global pharmaceutical companies.

Companies getting substantial part of their revenue (mainly contract manufacturing / custom synthesis) from CRAM services include: Nicholas Piramal (NPIL), Marksans, Aurobindo, Dishman, Wockhardt, Jubilant Organosys, Matrix Labs, Glenmark, Lupin Labs, Wockhardt, IPCA Labs, Kopran, Cadila Healthcare, Biocon, Bharat Biotech, Shasun Chemicals, Divis, Suven life sciences

In the last five years a number of companies (over 30) have come up offering contract research services including clinical research. These include companies like GVK bio sciences, Sipra labs, Vimta labs Triesta Sciences, Quintiles India, Neeman Medical International (NMI), Lotus Labs, iGate Clinical Research International, ARC -- Alembic Research Centre, Clinigene (a subsidiary of biocon)

The Indian pharmaceutical outsourcing market was valued at USD1.27m in 2007 and is expected to reach USD3.33 billion by 2010, growing at a CAGR of 37.6%. The Indian CRAMS market stood at USD1.21 billion in 2007, and is estimated to reach USD3.16 billion by 2010.

Emerging trends in the sector...

CRAMS market is witnessing a number of trends. While contract manufacturing (custom synthesis), comprising APIs and intermediates has been growing at a phenomenal pace

as close to 35 per cent, there are emerging areas like contract manufacturing of generic products, which will also pick up in the future. The clinical research market is also likely to undergo a composition change; bioavailability/bioequivalence studies have occupied a reasonable share of the clinical research market. However, clinical trials of NCEs / NBEs (Phase II–IV) and data management would pick up in the years to come.

In addition to that, value added services like method development, impurity profiling and characterization and stability studies plus formulation development and regulatory support with clinical trial supplies are some of the new opportunities

NOTES ON SERVICES

Clinical Research

Clinical trials involving new drugs are commonly classified into four phases. Each phase of the drug approval process is treated as a separate clinical trial. The drug-development process will normally proceed through all four phases (Now a 0 phase is also introduced) over many years. If the drug successfully passes through Phases I, II, and III, it will usually be approved by the national regulatory authority for use in the general population. Phase IV are 'post-approval' studies. The patient population is increased from phase to phase. It may start with 20 at phase I and go upto 3000 in phase III.

The services covered here is for phase I to Phase III trials. These could be for NCE or Generics. Major Market share trend is expected from generics. If the generic product is of the same dosage as the original drug, companies providing comparative study of the proposed product with original drug as value addition. **THESE TESTS INCLUDE BIO-AVAILABILITY, BIO-EFFICACY STUDIES.**

Formulation research

To carry out the clinical trials the drug has to be prepared in the required dosage form i.e. tablet, capsule containing specified dose. Before carrying out clinical trials companies will test the formulation for **Solubility And Stability**. Based on the results the method of formulation may be changed. This service is needed for NCEs and Generics. Here also the main market is generics.

Formulation manufacturing

Clients contracting services /showing interest to enter into contracts are asking companies to provide the formulation manufacturing service also. This will help the client to deal with one service provider and reduce the documentation related work. As most of the clients are looking for these services under one roof.

1.6. INVESTMENT

The investment (Project Cost) requirement for setting up a Clinical Trails, Formulation Development & Testing services and Manufacturing Support Services would be around Rs. 14.60 Crores and the breakup of the cost of the project is tabulated below.

1. Clinical testing services

2. Formulation development and testing services
 3. Manufacturing support services
- Clinical services: Maximum of 10 ~ 15 products / Projects (20 to 25 volunteers / project) per month
 - Formulation Development services: Maximum of 120 products / projects per year
 - Manufacturing Support Services (Tablets: 150 million / Annum, Capsules: 300 million / Annum)

Table 1: Project Cost

(Rs. Crores)

SI.No	Description	Min	Max	Avg
1	Land & Site Development (8 acres @ Rs. 25.00 Lakhs / acre)	2.00	8.00	5.00
2	Buildings & Civil Works	20.00	26.00	23.00
3	Plant & Machinery	36.00	40.00	38.00
4	Vehicles, Software Cost	1.00	1.00	1.00
5	Furniture & Fixtures	2.00	2.50	2.25
6	Office Equipment & Misc	3.00	3.50	3.25
7	Deposits	4.00	5.00	4.50
8	Pre-operative Expenses	8.00	12.00	10.00
9	Margin Money for Working capital	2.00	4.00	3.00
10	Total	78.00	102.00	90.00

Suggested means of finance is tabulated below.

Table 2: Means of finance

(Rs. Crores)

SI.No	Description	Min	Max	Avg
1	Equity from Promoters	26.00	34.00	30.00
2	Term Loan from FI's	52.00	68.00	60.00
3	Total	78.00	102.00	90.00

The debt equity is considered as 2 :: 1 with 66.66% as term loan.

The operations can reach 80% of its capacity within 3 years and can give employment of around 100 to 600 direct manpower.

1.7. RETURNS

The returns from the project are adequate enough to repay the term loan in 6 years time from the date of commercial operations. The key financial indicators of the project are tabulated below.

Table 3: Key Financial Indicators

Particulars	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6	Year 7
Total Income	24.00	31.00	38.00	46.00	52.00	57.00	61.00
Total Variable Costs	10.00	14.00	18.00	24.00	32.00	36.00	40.00

Total Fixed Costs	4.00	4.00	4.00	4.00	3.00	3.00	3.00
Total Expenditure	14.00	18.00	22.00	28.00	35.00	39.00	43.00
PBIDT	10.00	13.00	16.00	18.00	17.00	18.00	18.00
Profit Before Tax (PBT)	4.00	6.00	8.00	11.00	10.00	12.00	13.00
Profit After Tax (PAT)	3.00	5.00	6.00	7.00	7.00	8.00	9.00
Cash Accruals	5.00	9.00	10.00	11.00	12.00	11.00	11.00
BEP (Op Capacity)	75%	68%	57%	51%	47%	41%	35%
Gross DSCR	2.40	2.20	2.25	2.20	1.80	1.80	1.82
Average DSCR	2.00						
Average Net DSCR	2.70						
IRR	19%						
NPV	4 @ 15%						