

CHEMCON - 2002

CUSTOM CHEMICAL MANUFACTURING IN NORTH AMERICA

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PRESENTATION OUTLINE

- **Definitions of Custom manufacturing**
- **Market Overview of Custom Manufacturing in the U.S.**
- **An in-depth Look into the Fine & Pharmaceutical base chemicals**
- **Market Trends and Outlook**
- **Suppliers of Custom Manufacturing**
- **Profile of a Successful Custom Manufacturer**

DEFINITION

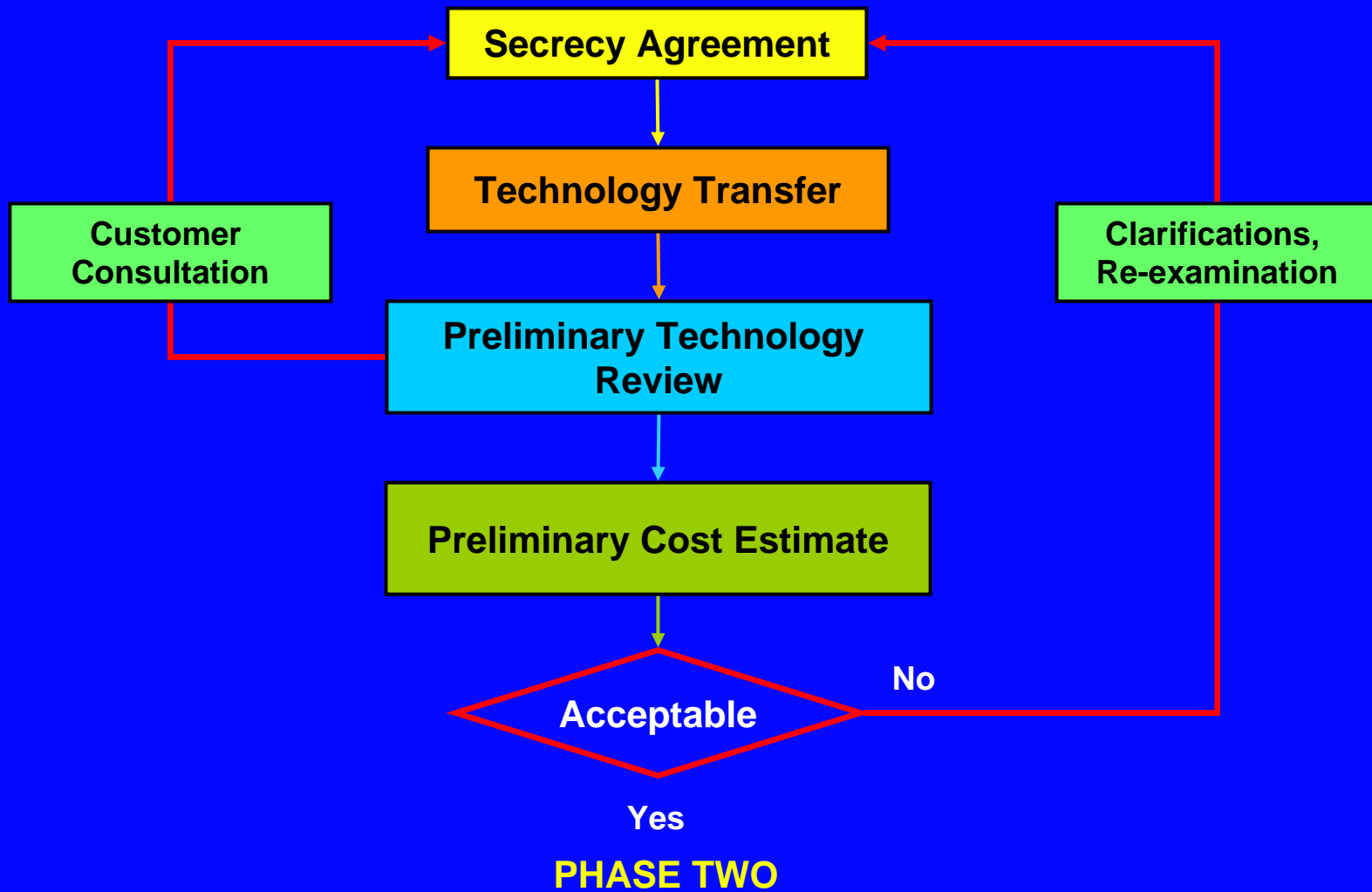
Custom Manufacturing is the dedication of production processing for a customer, in which the technology is provided by the customer himself. The production process, product quantity and manufacturing economics is tailor-made according to the customer's specifications.

DEFINITION

The definition of custom manufacturing can also be extended to toll manufacturing, where the customer provides all or part of the raw materials required.

This is particularly common when the customer or sponsor is a major producer in the industry. Toll manufacturing also involves the rental of equipment and production personnel (e.g. lab technicians, engineers etc.) on a laboratory scale. The scale-up production, however, is supplied by the sponsor company i.e. the customer.

PHASE I



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PHASE I

STEP 1: SECRECY AGREEMENT

Confidentiality is the most crucial element in the transaction between the custom manufacturing supplier and customer.

The terms of the agreement may be unique for each supplier-customer relationship but still maintains some standard items. Basically, the CDA stipulates that any information disclosed orally, whether unilaterally or bilaterally, should be disclosed within 6-12 months of the implementation of the CDA. The non-disclosure period can be any where from 10 – 20 years.

The initiator of the agreement is usually the party whose technology needs to be protected. The time required to review the secrecy agreement may vary widely depending on the project's urgency.

PHASE I

STEP 2: TECHNOLOGY TRANSFER

Technology transfer can be partial or complete. Partial transfer may simply involve a brief description of the chemistry whereas a complete transfer will involve a thorough writing of every operating procedure with a full toxicity and hazards package.

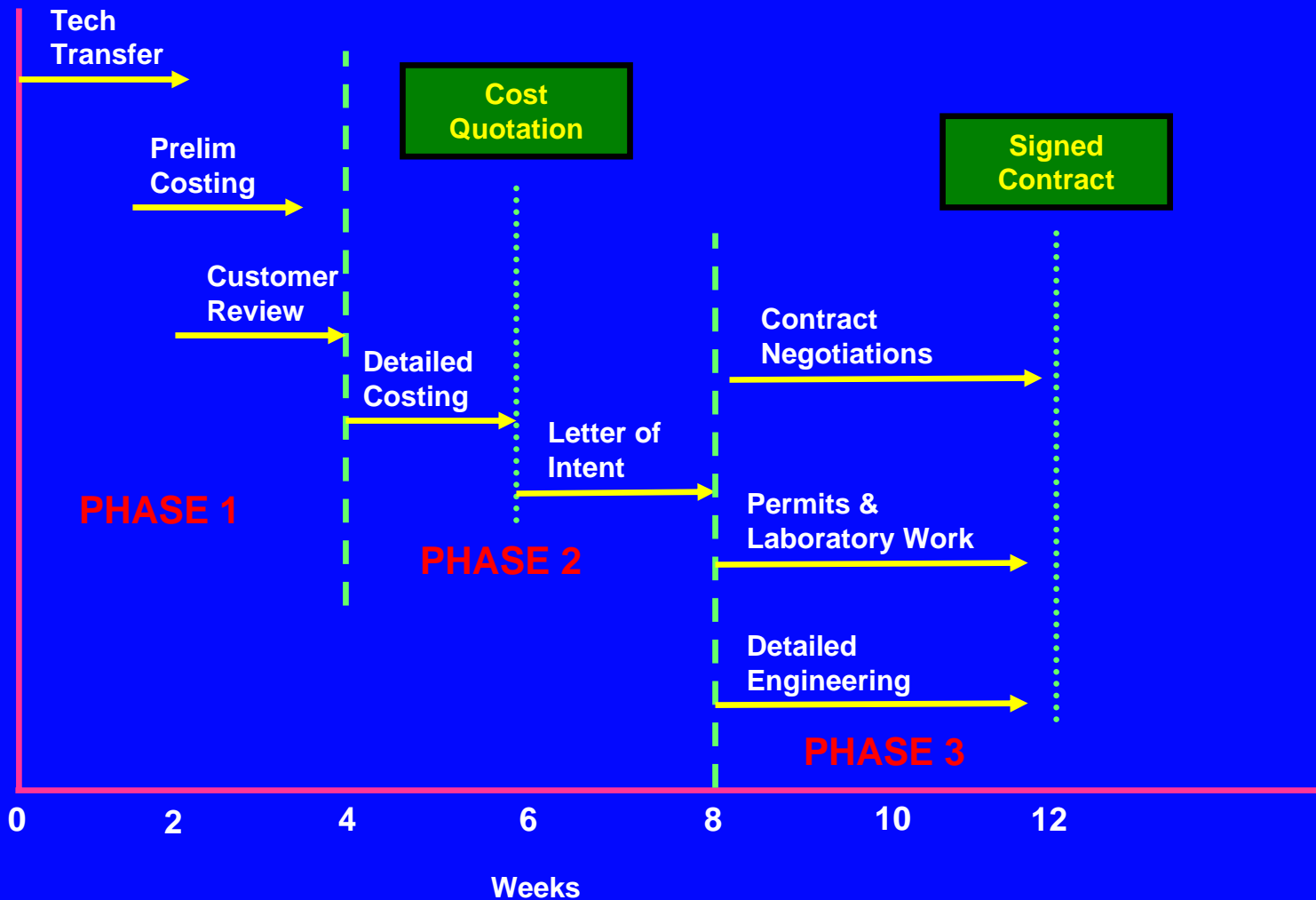
Due to the risks of disclosing proprietary technology knowledge, the execution of the CDA will always precede full disclosure.

STEP 3: TECHNOLOGY & COST REVIEWS

At this point, the technology is more closely evaluated by the Operation & Development department to determine the feasibility of the project. A cost estimation of the technology package provided by the custom manufacturer is given in the preliminary review.

TIMELINE

Customer Inquiry



PHASE I

LETTER OF INTENT

While contract negotiations are underway, a signed letter of intent will initiate developmental laboratory work, permit applications and detailed engineering procedures. Permit applications can be quite time consuming depending on the type of material produced and wastes generated. For example, if VOCs or any regulated waste chemicals are emitted, an Air Quality Permit will have to be obtained and this process can take up to 3 months. If the emission volumes are minimal, the application process may take less time.

PHASE I - TIME LINE

Signed Contract

Permits

Laboratory Work

Equipment Purchase, Modification & Setup

Procedures, HAZ-OP & Training

START-UP

Review & Modifications

Stable Process

PHASE 3

PHASE 4

12 14 16 18 20 22 24

Weeks

10



PHASE III

LABORATORY WORK

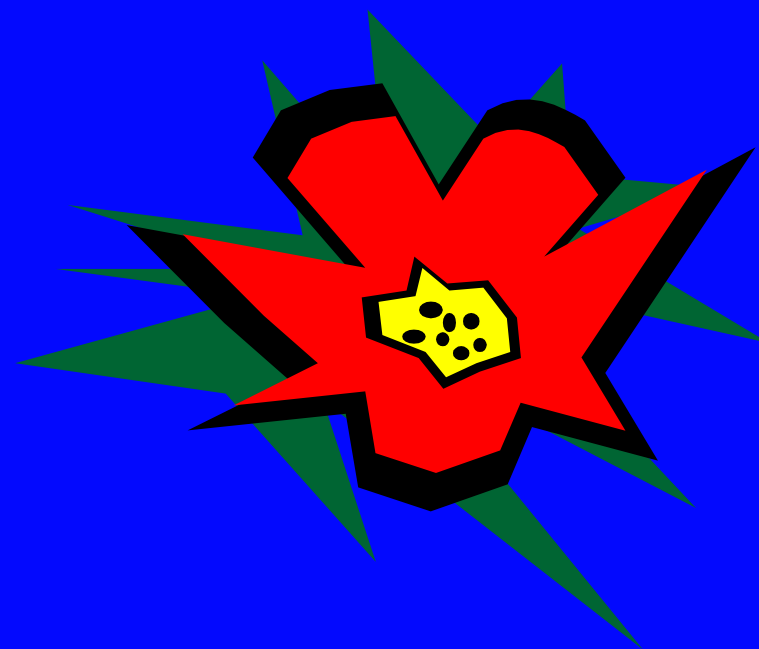
In phase 3, equipments are installed (if required) and the Operating Procedures will be completed. The laboratory phase is crucial in verifying the true feasibility of the production (prior to scale-up) and in determining the optimal conditions. Scale-up plans are also made in conjunction with the laboratory operation if required. A HAZ-OP is performed with all the personnel including chemists, engineers and technicians. Each step of the operating procedure is reviewed in order to fully understand all safety and environmental issues associated with the production.

The operators will also be trained at this stage to handle a full scale plant.

PHASE IV

START UP

The process is run at full capacity and the full contract should be finalized at this stage. The quality of the products are evaluated before production continues after the first batch.



WHY CUSTOM MANUFACTURING?

❑ **SPEED** – A reputable custom manufacturer that have the right equipment and technical expertise can help a customer bring the products to the market within a much shorter time frame. Additional equipment can be bought and installed faster. Essentially, this translates into earlier sales and a competitive edge for the customer.

❑ **RISK REDUCTION** – Custom manufacturing is especially beneficial when a producer is merely ‘testing the waters’. Before bringing a product line into full commercialization, the producer may prefer producing smaller quantities of the product instead of risking full capital investments in a dedicated plant facilities, human resources and marketing.

WHY CUSTOM MANUFACTURING?

- ❑ **PRODUCTION EXPERIENCE** – Before designing a full-scale plant, a custom manufacturer can work with the customer in the experimental stages to fine-tune the design at a later time.
- ❑ **PERMITS** – A custom manufacturer who has already acquired specific permits for the production of certain materials will save its customer precious time in applying for the same permits. A large producer would turn to a custom manufacturer if the material produced involves sensitive environmental or health issues.
- ❑ **LOWER OVERHEADS** – As no large capital investments are required, custom manufacturing is a cost efficient way for producers to manufacture products in smaller volumes.

OVERVIEW OF NORTH AMERICAN CUSTOM MANUFACTURING INDUSTRY

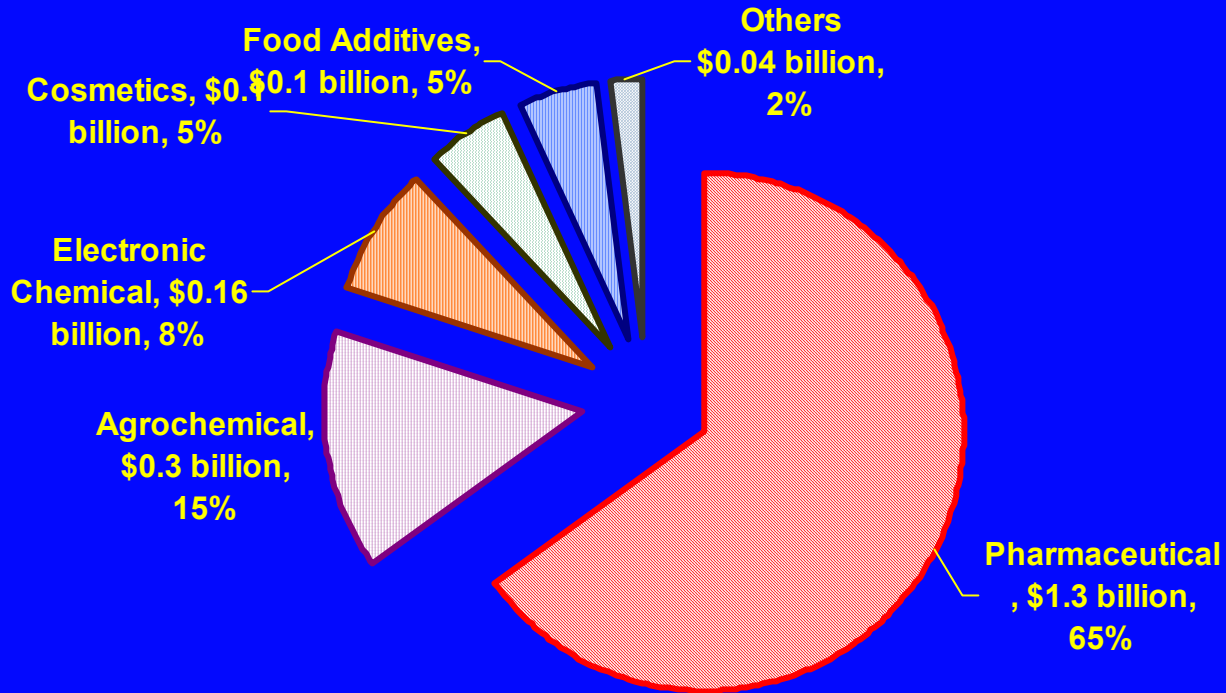
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THE MARKET OVERVIEW

- **The custom manufacturing market is estimated to have a value of \$10 billion globally and U.S. vendors account for only \$2 billion. Europe has always been in the forefront of this this business. The emergence of the outsourcing market in the U.S. has been encouraging in recent years due to a variety of factors. Before going into an in-depth discussion, the breakdown of the industries by type in custom manufacturing is shown in the following chart.**
- **Pharmaceuticals account for nearly two thirds of the business followed by agrochemicals and other specialty chemicals such as fragrances, flavors etc.**
- **The industry is estimated to grow at 6 -7 % although the current growth rate is only 2% due to the sluggish economy. This is further aggravated by product failures in the developmental phases or overcapacity problems.**

BREAKDOWN OF CUSTOM MANUFACTURING BY INDUSTRY TYPE, NORTH AMERICA, 2001



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**Total Market Value for Custom Manufacturing,
NA = US\$ 2 Billion**

PHARMACEUTICALS

Drug companies outsource some of their manufacturing needs due to the following reason:

- **New medicines with no commercial track record do not justify major capital investments.**
- **Many U.S. custom manufacturers have multi-purpose cGMP capability, offering a wide array of process technologies and technology services.**
- **The drug development timetable from research phase to commercialization phase has shortened considerably as drug companies are heavily dependent on an attractive pipeline to lure investors.**
- **The “2000 by 2000” concept is the buzzword in the pharmaceutical community recently. This basically means that drug development time should not exceed 2000 days (5 ½ years) by the year 2000.**
- **Development of combinatorial and chiral chemistries. AS drug companies continue to churn out new pipelines, there are several new drugs to be tested. Hence, outsourcing can move these to the market faster.**

PHARMACEUTICALS

INTRODUCTION – CONT'D

- **Drug companies turn to outsource some of their manufacturing needs due to the following reason:**
 - 6. Many pharma companies do not have a wide range of highly specialized capabilities with regards to chiral chemistry.**
 - 7. Custom manufacturing companies now represent a convenient one-stop shopping service where smaller to mid-sized companies can utilize the facilities and technical packages offered from clinical to commercial quantities.**
 - 8. The speed at which products can be introduced to the market is accelerated through outsourcing. This enables large drug companies to market three to five blockbuster products a year.**

PHARMACEUTICALS

OUTLOOK

- **Drug companies have been suffering from declining revenues due to the following reasons:**

- 1. Notable product withdrawals**
- 2. Poor macroeconomics and declining equity markets**
- 3. Unimpressive pipelines with less than bright prospects of blockbuster launches.**
- 4. Less than 80 NME (New Molecular Entities) will be launched between 2003-2005.**
- 5. Drug output will matched the investments in R & D.**
- 6. Poor productivity in drug discovery, as new drugs are terminated in the early developmental stages.**

- **Hence, the custom manufacturing industry has suffered along with the pharmaceutical industry.**

CURRENT TRENDS

CURRENT MARKET

- **The robust growth of the custom manufacturing industry in the late 1990s can be attributed to the pharmaceuticals sector.**
- **The fundamental reason for the emergence of U.S.-based custom manufacturing capacity is the rapidly evolving drug industry.**
- **The custom manufacturing industry in the U.S. expanded as the pharmaceutical sector continued to show promising double-digit growth during the 1990s.**
- **The picture has not been rosy for the last few years as revenues declined resulted in industry consolidations.**
- **Overcapacity resulted when vendors continue to add capacity despite slowing demand.**
- **Some vendors such as Eastman has exited the fine chemical business due to increasing pricing pressures and very tight margins.**

WHERE ARE WE HEADED?



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FUTURE TRENDS

FUTURE TRENDS

- **Increased competition from Asia has also intensified the competition in the custom manufacturing industry.**
- **The year 2002 is seen as a transitional period as drug companies continue to battle with increasing pressure from generics in traditional blockbuster products, marketing and product investments.**
- **Although market performance has been mediocre in 1999-2000, many are optimistic of future spending in product launches.**
- **The landscape for custom manufacturing will mainly be dominated by small and medium players who have continued to focus on complex chemistry, a service much needed by large pharma companies.**

FUTURE TRENDS

FUTURE TRENDS

Volume demand for the pharmaceuticals sector is expected to grow at 7%.

Biotechnology will become the next important source of revenues as most bio-tech start-ups are very dependent on contract or toll manufacturing

Due to limited resources. Biotech companies turn to 'kilo-shops' for products in the early developmental stage.

Start-up drug or biotech firms have become significant contributors to the custom manufacturing business. The 'kilo-shop' concept has been gaining popularity because all production work is done on a laboratory scale with minimal overheads, hence translating into greater savings for customers.

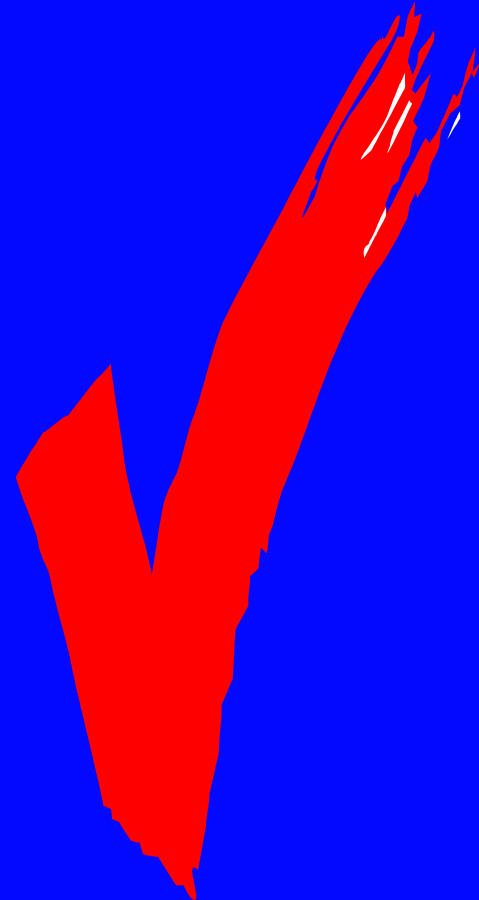
FUTURE TRENDS

FUTURE TRENDS

- **A wide variety of molecular platforms with increased complexity will warrant the services of custom manufacturers.**
- **The rapid pace of drug discovery and development in the pharmaceutical industry will continue to support the custom manufacturing business as more drugs will have to go through the initial testing period.**
- **Higher value drugs targeting specific diseases will characterize the market in the future. Outsourcing will continue to be a viable option as producers want to minimize risks and achieve maximum cost efficiency.**
- **The agrochemical market is expected to pick up from 2003 since the removal of Roundup Ready crops, which has prompted the removal of several products.**

THE PLAYERS

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THE PLAYERS

- There are three categories of custom manufacturers based on their sales revenues.

FIRST TIER
> US\$150 MILLION

Bayer/ChemDesign, DSM Fine
Chemicals, Fine Organics, Lonza,
Catalytica, Avecia

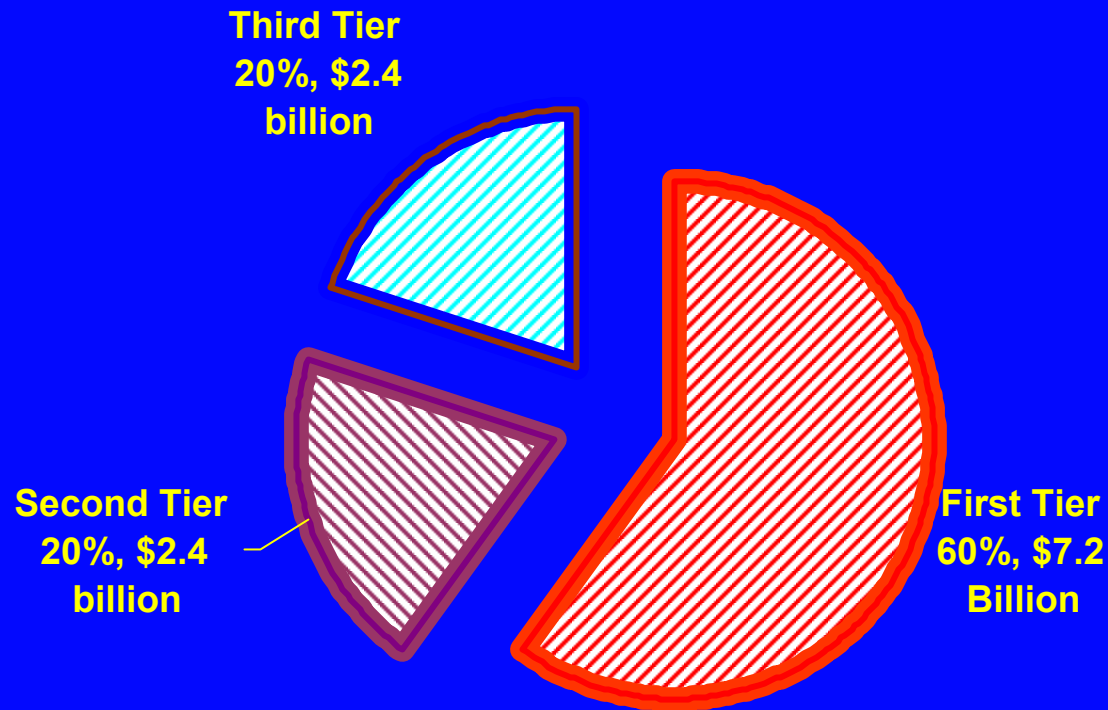
SECOND TIER
US\$100-\$150 MILLION

Ems-Dottikon, Omnicem,
Finorga, Hovione, Orgamol

THIRD TIER
~ US\$10 MILLION

Small companies

MARKET SHARES OF CUSTOM MANUFACTURERS, GLOBAL



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Total Market Value for Custom Manufacturing, Global = US\$ 12 Billion

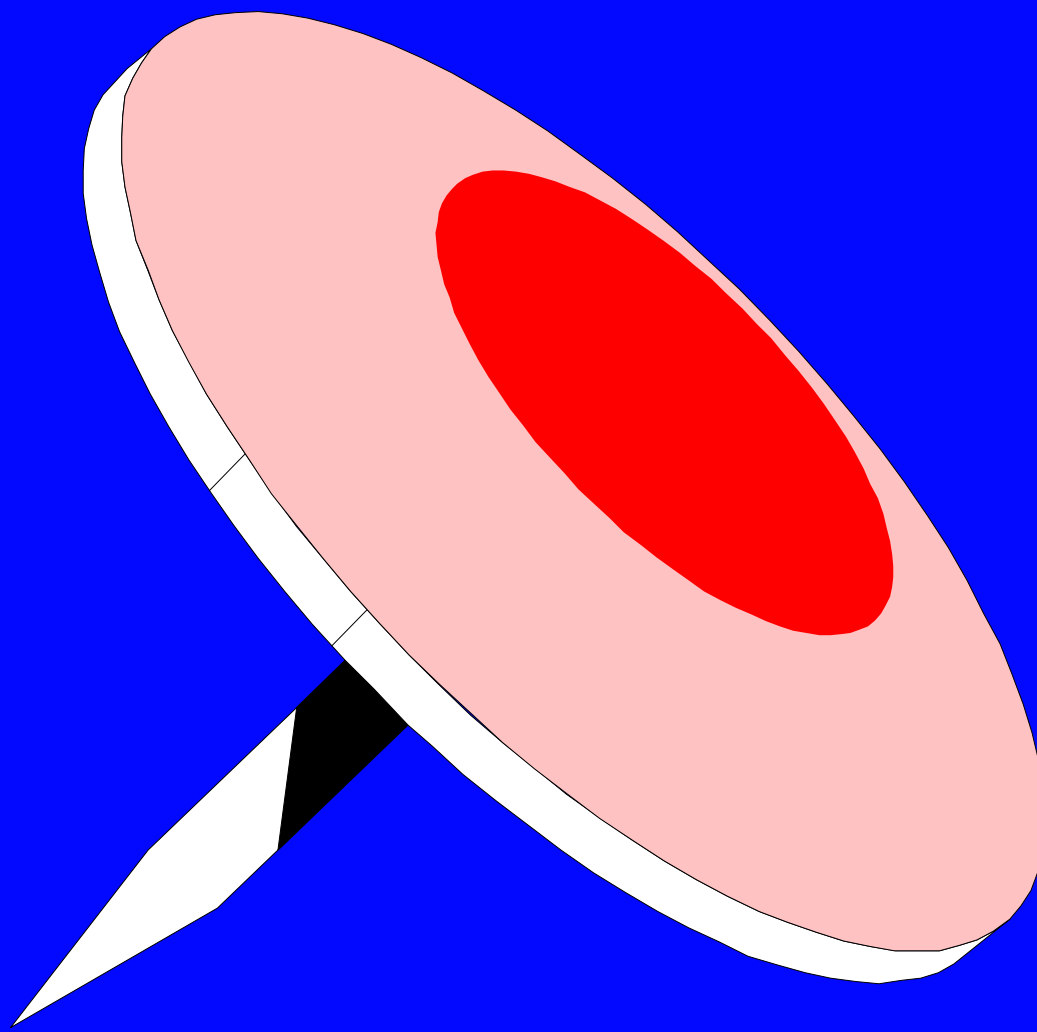
THE PLAYERS

- **Larger companies have more resources and broader range of manufacturing capabilities. Smaller companies typically have the competitive advantage of flexibility in adapting to customer needs and are less bureaucratic. A summary of the comparison between small and large companies is provided on the following slide.**
- **A typical contract package will include :**
 - 1. Process research**
 - 2. Regulatory support**
 - 3. Commercial manufacture (if feasible, depending on the size of the provider)**
 - 4. Flexibility in technology transfer (partial or complete)**
 - 5. Capable staff of chemists, engineers, technicians etc.**

THE PLAYERS

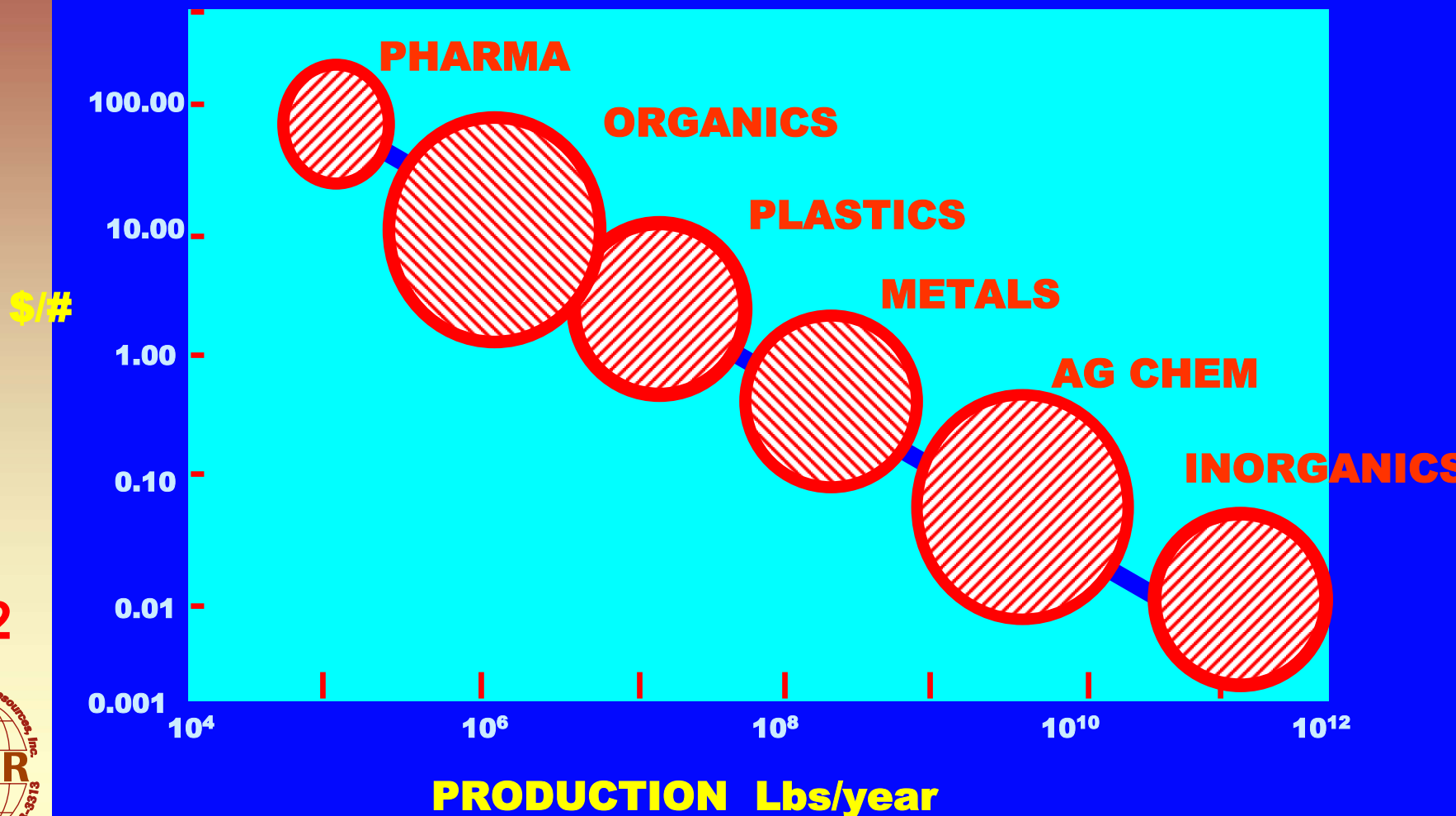
	Small	Large
Management	<ul style="list-style-type: none"> • Quick focused decisions 	<ul style="list-style-type: none"> • Complex decision making process • Possibility to pool important resources on one project
Marketing	<ul style="list-style-type: none"> • Personal contacts of top management • Small man-power 	<ul style="list-style-type: none"> • Global network • Skilled organization • Profound chemical/technical knowledge and expertise
Financial	<ul style="list-style-type: none"> • Profits are reinvested 	<ul style="list-style-type: none"> • Competition for funds with other divisions • Complex approval processes • More financial resources
Manufacturing	<ul style="list-style-type: none"> • Simple plants • Limited versatility in multipurpose facilities 	<ul style="list-style-type: none"> • Broad technological capabilities • Economy of size • Possibility to handle complex projects
R & D	<ul style="list-style-type: none"> • More suitable for transfer of developed processes 	<ul style="list-style-type: none"> • Bureaucratic risks • Able to manage complex projects

A SUCCESSFUL CUSTOM MANUFACTURER



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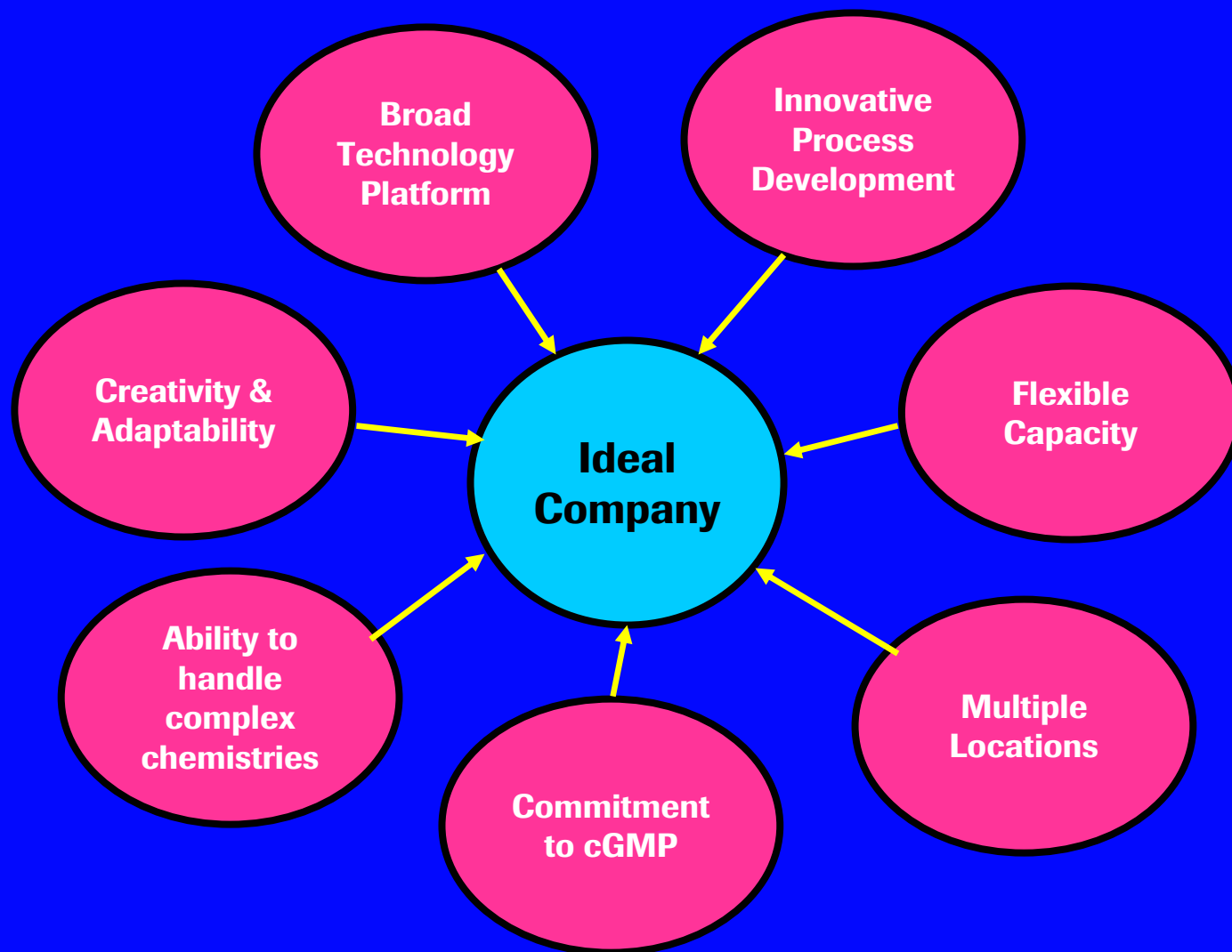
Custom Chemicals Provide More Opportunities



Custom Chemicals Provide More Opportunities

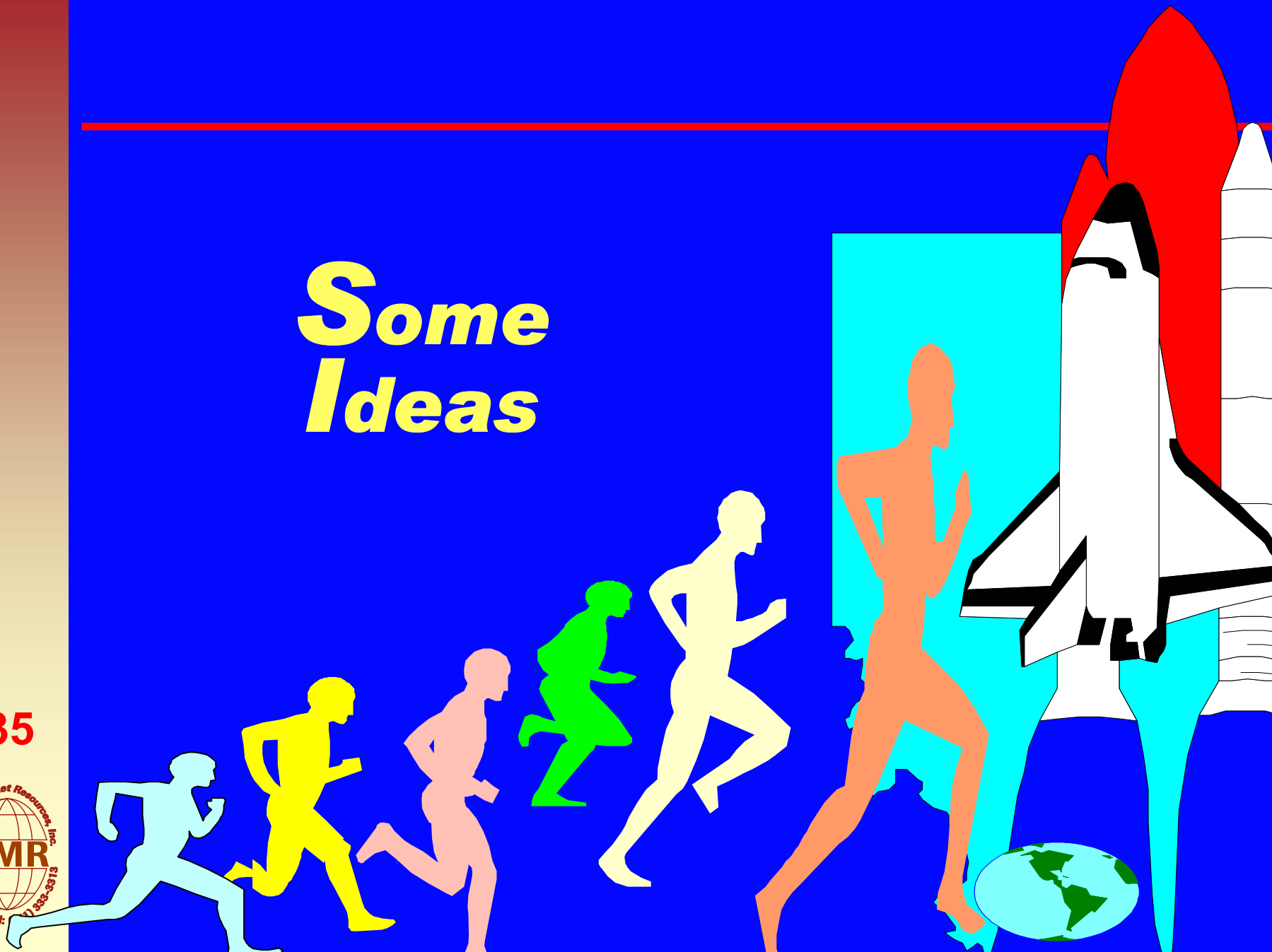
- **Less Infrasture**
- **More Knowldege**
- **Less Labor**
- **Less Investment**
- **Value Addition**
- **Distribution costs are higher**
- **Proivde oportunities for more participants**

SUCCESSFUL CUSTOM MANUFACTURER



Some Ideas

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WHY IS INDIA ATTRACTIVE?

- **India offers on the average more educated workforce than most of the other countries at a lower cost**
- **Most of the custom manufacturing opportunities are less capital/equipment intensive and more “educated labor” intensive**
- **Indians are more entrepreneurial - and intellectual**
- **Most Important – Thanks to the British legacy, we speak English – the universally accepted language**

ISSUES

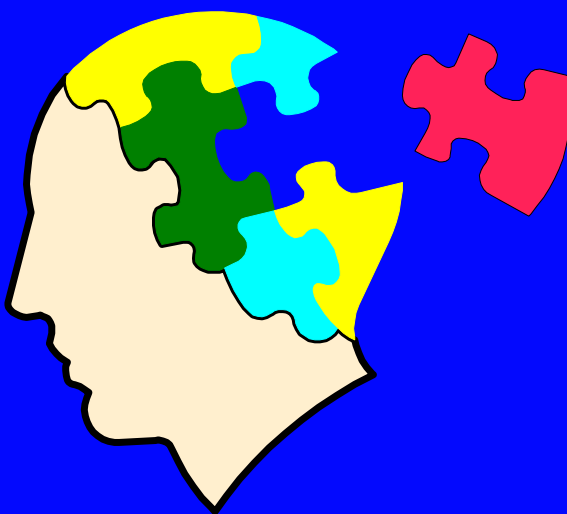
- **INTELLECTUAL PROPERTY**
- **COMMUNICATIONS AND INFRASTRUCTURE**
- **FOR AN OUTSIDER, DOING BUSINESS WITH/IN INDIA SEEMS VERY COMPLEX**

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- ◆ **Develop Relationships**
 - ◆ **American Companies are looking for people to work with**
 - ◆ **Address the IP issues Carefully**
 - ◆ **Indian chemical executives and managers are your best bet – Technical people have less influence.**

RECOMMENDATIONS

- **WORK WITH SMALL TO MEDIUM COMPANIES IN NORTH AMERICA**
- **DEVELOP LONG-TERM RELATIONSHIPS**
- **MARKET – MARKET – MARKET**
- **GO MEET PEOPLE IN PERSON**
- **NORTH AMERICA, UNLIKE MOST ASIAN COUNTRIES DOES NOT DEPEND ON “AGENTS” – THEY PREFER DIRECT APPROACH**
- **COMMUNICATE, CONVINCe, SELL SELL!**

THANK YOU FOR YOUR ATTENTION!



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