Chapter 4

UNDERSTANDING FACT-MAKING AND THE QUALIFICATION OF DRUGS IN AN INDUSTRIAL LABORATORY: A VIEW FROM THE BENCH

This chapter essentially examines the process of fact-making or knowledge production and the ‘qualification’ of drugs in a pharmaceutical firm, Dr Reddy’s Laboratories, through an interrogation of the every day practices and routines of the scientists in its discovery research centre in Hyderabad. The chapter begins with a brief history of the firm. It then undertakes a profiling of the activities of the firm, with a special focus on its basic research and patenting activities, drug testing activities, the therapeutic areas the firm deals in and its markets. Subsequently, through the narratives of three key informants\textsuperscript{88} in the firm, it provides a descriptive account of how the scientists in the firm, interact with each other in an interdisciplinary context, to transform indeterminate and amorphous problems in the laboratory into concrete entities that have therapeutic value. In

\textsuperscript{88} Permission for interviews with other employees in the firm was not granted. The details have been mentioned in Chapter 2 on the methodology used for the study. Nevertheless, detailed interviews were carried out with each of these three key respondents. About four rounds of taped interviews were carried out with Respondent 1, the ex-R&D Head of the firm. Two of these were carried out in November 2005 and February 2006, during his tenure as Vice-President (Discovery Research) in the organization and two interviews were carried out after his exit from the organization. Two rounds of taped interviews were carried out with Respondent 2, the present Vice President (Toxicology) of the firm, one in November 2005 and the other in May 2008 and one detailed taped interview was done with Respondent 3, the present Vice-President (Discovery Research) of the firm in May 2008. These respondents are key informants, since in addition to occupying managerial positions and witnessing several strategic decisions taken by the firm; they have also spent a considerable number of years on the bench since the inception of drug discovery in the Indian industry. Respondent 1, a highly reputed medicinal chemist, was with the firm during the period 1998-2006. Prior to his joining the firm, he was a Director at a CSIR lab and post his exit from the firm in late 2006, now heads a prominent institute in Hyderabad, which engages in cutting edge basic research in the pharmaceutical sciences. Respondent 2, a toxicologist, has been with the firm since the early nineties, when the firm first initiated efforts in drug discovery and has been a vital part of the firm’s early successes and failures in this regard. Respondent 3 joined the firm relatively recently. He has about 15 years of experience in multinational firms, both in India and mostly abroad. He enjoys considerable repute in the fields of clinical development and bioinformatics. These interviews were mostly carried out in the period from November 2005-March 08. Two interviews were carried out in May 2008. The case study also draws upon the insights derived from firm-related documents such as investor reports and annual reports and interviews carried out with nineteen respondents from nine other large-scale firms, six of which are engaged in discovery research in the Indian pharmaceutical industry. Though these three respondents have highlighted several important processes relating to discovery research and testing in their firm, they have clarified that these views have been stated in their individual capacity as scientists and do not represent the views of the company.
doing so, it also examines how these drugs are attributed with certain ‘qualities’, which
determine their fate as ‘candidates’ for further testing on human beings and vest them with
the potential for eventual commercialization.

**Brief History and Profile of activities of the Company**

The company was incorporated in India by its promoter and its current Chairman,
Dr. K. Anji Reddy as a Private Limited Company on February 24, 1984. The firm was
converted to a Public Limited Company on December 6, 1985 and listed on the Indian Stock
The firm is credited with having several firsts in different arenas. In 1997, it was one of the
first to out-license a molecule to a multinational company for clinical development. In the
mid-nineties, it became the first firm to enter the U.S. generics market and in 2007, it
became the first firm to hive off its R&D centre from its other concerns as part of the
company strategy to mitigate risks associated with drug discovery.

The firm began its career through the supply of bulk drugs to Indian manufacturers.
It soon graduated to the export of these active ingredients to other less regulated markets
outside the country. These unregulated markets also operated in a process patent regime like
India. This enabled the company to build and consolidate its strengths in reverse
engineering. The early nineties were witness to the company beginning formulation units
and entering into joint ventures in Russia and the Middle East.

However, by the early-nineties, the firm had begun to focus on obtain US-FDA
approval for its bulk drug and manufacturing units in order to enter the generics market in
the United States. The objective of the company was, however, to transition into a discovery
research based firm, along the lines of firms in the West. According the discovery research
centre in Hyderabad, Dr Reddy’s Research Foundation, was set up in Hyderabad in 1992. In 1996, the firm filed its first US patent. In 1997, the firm came up with the insulin sensitizer molecule, DRF 2593, which was outlicensed to Novo Nordisk. It outlicensed the second molecule, DRF 2725, to Novo Nordisk in 1998. In 2001, the firm launched its first generic product with market exclusivity in the United States and received approval from US-FDA to market Eli Lilly’s anti-depressant, Prozac.

In 2002, the firm entered into the European market through the acquisition of BMS Laboratories in the United Kingdom. However, in 2003, the firm’s discovery efforts received a setback when Novo Nordisk suspended clinical trials on both the outlicensed molecules. However, by 2004, the firm had established it’s market presence in 40 countries, filed around 39 ANDAs (Abbreviated New Drug Applications) and come up with six other new chemical entities in different therapeutic areas.

In September 2006, the firm entered into an agreement with ClinTec International for the joint development of an anti-cancer compound, DRF 1042, for use as potential treatment of various types of cancer. The firm has completed Phase I clinical trials for DRF 1042 in India. According to the terms of this agreement, DRL and ClinTec International will co-develop DRF 1042 and undertake Phase II and Phase III clinical trials, in order to secure U.S. FDA and European Agency for the Evaluation of Medicinal Products (EMEA) approvals. As per the agreement, the firm has granted ClinTec International the commercialization rights for most of Europe, including major European markets, and the firm retains the commercialization rights for the rest of the world, including the United

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89 The last section of this chapter deals with this out-licensing episode in detail
States. Following commercialization of the product, the firm will receive a royalty on sales by ClinTec.

In September 2005, the firm announced the formation of an integrated drug development company, Perlecan Pharma Private Limited as a joint venture with Citigroup Venture Capital International Growth Partnership Mauritius Limited and ICICI Venture Funds Management Company. The terms of the joint venture were amended in March 2006. Under the terms of the joint venture agreement, CVC and ICICI Venture contributed Rs.1 018 million each and the firm contributed Rs.170 million towards Perlecan’s initial equity capital. Furthermore, the agreement granted DRL the first right to conduct product development and clinical trials on behalf of Perlecan Pharma on an arm’s length basis. In 2007, the firm entered into a Research Services Agreement with Perlecan Pharma according to which the firm provides Perlecan Pharma with clinical development support and services.⁹⁰

The firm has collaborated with the National Cancer Institute in Maryland, an institute which is part of the United States’ National Institutes of Health. In February 2006, the firm entered into an agreement with Argenta Discovery Limited for the joint development and commercialization of a novel approach to the treatment of Chronic Obstructive Pulmonary Disease (COPD). Under the terms of the agreement, the parties agreed to collaborate to identify clinical candidates from a certain class of the firm’s compounds for use as potential treatments for COPD. Both parties agreed to jointly develop the selected candidates from the pre-clinical stage up to Phase IIa (proof-of-concept). Upon successful completion of a Phase

IIa trial, each of the parties may either license-out the candidate for further development and commercialization to a larger pharmaceutical company or continue the further co-development and commercialization themselves. The firm and Argenta have agreed to fund the joint collaboration up to proof-of-concept and share the development expenses equally and profits at a predetermined ratio. DRF 2546 was identified as candidate that could be developed for COPD, and preclinical development has begun in this regard.\footnote{Ibid}\footnote{223}5\footnote{35.5}

In the context of charting out the above history of the firm, it would be pertinent to offer a brief glimpse into its activities. Chart 4.1 depicts the proportion of the firm’s revenues through different activities such as sales of formulations, API, generics, critical care and biotechnology and drug discovery and custom pharmaceutical services for the year 2007. The data reveals that the firm obtains a major portion of its revenues from the sales of generics.

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{chart41.jpg}
\caption{Proportion of the firm's revenues through different activities in 2007}
\end{figure}

Table 4.1 depicts a profile of the firm’s sales in India in terms of revenues and products in different therapeutic categories for the year 2007. The data shows that the firm obtains the maximum revenue from sales of its cardiovascular formulations, followed by formulations in the therapeutic categories of gastrointestinal related complaints, pain management and diabetes management.

<table>
<thead>
<tr>
<th>Therapeutic Category</th>
<th>No of Products</th>
<th>Revenues (Rs. In million)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiovascular</td>
<td>45</td>
<td>1222.5</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>35</td>
<td>1292.1</td>
</tr>
<tr>
<td>Pain Management</td>
<td>20</td>
<td>968.4</td>
</tr>
<tr>
<td>Diabetes Management</td>
<td>25</td>
<td>479.9</td>
</tr>
<tr>
<td>Neutraceuticals</td>
<td>13</td>
<td>324.0</td>
</tr>
<tr>
<td>Anti-Infectives</td>
<td>21</td>
<td>367.6</td>
</tr>
<tr>
<td>Dermatology</td>
<td>16</td>
<td>285.6</td>
</tr>
<tr>
<td>Dental Care</td>
<td>23</td>
<td>235.5</td>
</tr>
<tr>
<td>Urology</td>
<td>16</td>
<td>205.9</td>
</tr>
<tr>
<td>Respiratory</td>
<td>3</td>
<td>172.4</td>
</tr>
<tr>
<td>Gynaecology</td>
<td>9</td>
<td>126.7</td>
</tr>
<tr>
<td>Others</td>
<td>38</td>
<td>734.4</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>274</strong></td>
<td><strong>6415.0</strong></td>
</tr>
</tbody>
</table>


Table 4.2 gives a profile of the current discovery related activities of the firm and the alliances in relation to these activities. The discovery of new chemical entities is in the therapeutic categories of metabolic disorders, cardiovascular ailments and oncology segment.

<table>
<thead>
<tr>
<th>New Chemical Entities currently under development</th>
<th>Metabolic disorders</th>
<th>Phase II completed</th>
<th>Rheosine</th>
<th>Long-term carcinogenicity studies completed. Entered Phase III clinical testing in July 2007.</th>
</tr>
</thead>
<tbody>
<tr>
<td>DRF 2593</td>
<td>Metabolic disorders</td>
<td>Phase II completed</td>
<td>Rheosine</td>
<td>Completed Proof of Concept for Type IV/V dyslipidemia.</td>
</tr>
<tr>
<td>DRF 10945</td>
<td>Metabolic disorders</td>
<td>Phase II in progress</td>
<td>Assigned to Perlecan</td>
<td>Perlecan inducer for the treatment of atherosclerosis.</td>
</tr>
<tr>
<td>RUS 3108</td>
<td>Cardiovascular</td>
<td>Phase I completed</td>
<td>Assigned to Perlecan</td>
<td>Entered Phase II clinical testing in April 2008.</td>
</tr>
<tr>
<td>DRL 16536</td>
<td>Metabolic</td>
<td>Phase I in progress</td>
<td>Assigned to AMPK modulator for the treatment of diabetes.</td>
<td></td>
</tr>
</tbody>
</table>
Table 4.3 provides a profile of the USPTO, PCT and India based patents filed by the firm and granted in various therapeutic areas. The largest number of patents were filed by the firm and granted to it in the diabetes segment.

<table>
<thead>
<tr>
<th>Category</th>
<th>USPTO Filed</th>
<th>USPTO Granted</th>
<th>PCT Filed</th>
<th>PCT Granted</th>
<th>India Filed</th>
<th>India Granted</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anti-diabetic</td>
<td>68</td>
<td>39</td>
<td>60</td>
<td>110</td>
<td>30</td>
<td></td>
</tr>
<tr>
<td>Anti-cancer</td>
<td>13</td>
<td>8</td>
<td>12</td>
<td>43</td>
<td>12</td>
<td></td>
</tr>
<tr>
<td>Anti-bacterial</td>
<td>7</td>
<td>4</td>
<td>7</td>
<td>20</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Anti-inflammation/Cardiovascular</td>
<td>33</td>
<td>9</td>
<td>13</td>
<td>14</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Anti-ulcerant</td>
<td>1</td>
<td>1</td>
<td>—</td>
<td>1</td>
<td>—</td>
<td></td>
</tr>
<tr>
<td>Miscellaneous</td>
<td>4</td>
<td>1</td>
<td>3</td>
<td>23</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>TOTAL</td>
<td>126</td>
<td>62</td>
<td>95</td>
<td>211</td>
<td>50</td>
<td></td>
</tr>
</tbody>
</table>

(2) “PTC” means the Patent Cooperation Treaty, an international treaty that facilitates foreign patent filings for residents of member countries when obtaining patents in other member countries.


Narratives of the Key Informants

The following section provides a descriptive account of the strategies related to drug discovery and testing pursued by the firm and its everyday practices and routines. The narratives of the respondents largely chronicle the research practices and routines of the firms in the period from late 2005 to 2008. In addition, they dwell on the research practices of the firms in its early years, particularly with reference to its early strategy of out-licensing its molecules to a multinational firm. More importantly, the section also examines how in the process of producing facts related to drugs, at the bench, the scientists imbue these drugs with certain ‘qualities’ or ‘attributes’, which are shaped equally by techno-scientific and commercial concerns.
Strategies on Research Portfolio and Choice of Therapeutic Areas

The firm focuses on basic research in ‘life style management’ diseases like diabetes, cardiovascular related diseases, metabolic syndromes and obesity. These diseases demand a longer duration and sometimes even a life time of treatment and are therefore seen as more lucrative in the long term by the firm. It essentially seeks to target and capture a slice of the huge market for these diseases in Europe and the United States and also the emerging market in India. As respondent 3 remarked,

For a pharmaceutical company to succeed, especially for a company which is in drug discovery it is important for them to look into the projects which are going to rewarding in a long term. And being a very competitive area today, every successful pharmaceutical company aspires to get a major share from the markets across the world. Right. US and Europe happen to be two major markets because, especially, some lifestyle management diseases are prevalent in these societies. Cardiovascular area is under the purview of metabolic syndromes. Metabolic syndrome is a group of five different entities. So any one of those entities can be classified under metabolic syndrome. These therapeutic areas are not necessarily final ones, but currently we are working on diabetes, cardiovascular, metabolic syndromes, obesity. It’s not to say that it’s going to be restricted to these areas. We are in the process of expanding into other areas.

The trope of ‘unmet medical needs’ constantly figures in pharmaceutical scientists’ discourse in relation to their relatively late entry into discovery research in comparison to firms in the West, their choice of therapeutic areas and their keen interest in engaging in discovery work in life-style management diseases. Interestingly, this discourse of ‘unmet medical needs’ is deployed in relation to the disease profile of the markets that they seek to target92 rather than global disease patterns, which clearly indicate that more that 80% of the world population suffers from infectious diseases.93

In the nineties, the domestic firms here felt they had to be on the global map, they should have their own identity by making new molecules, the criteria then was to address unmet medical needs, one can ideally work on whatever one likes, but globally the criteria of unmet medical needs exists when it comes to chronic

92 Which pertains to life style management diseases
diseases. The duration of the treatment is long in chronic diseases and there is always a scope to give better medicine in diseases like diabetes, cancer etc. So that was our motivation for entering into basic research. So with this objective, we started this centre in 1994, to look into oncology, diabetes, cardiovascular, hypertension etc.

In this connection, Respondent 1 highlights the firm’s motivation to take up research in the area of diabetes. The respondent points out the growing incidence of the disease not only in Western countries but also world-wide, including India. Scientific interests are clearly tailored to the therapeutic demands of the market. The respondent’s remarks capture the firm’s anxieties in relation to its survival in the post-patent regime and the ‘foresight’ of its founder in venturing into a potentially lucrative therapeutic area.

When I say lifestyle management diseases, Diabetes comes to my mind because it is afflicting a very large proportion of the population worldwide. It is generally considered to be a disease of the modern world in the sense that people’s lifestyles have changed. Diabetes is an area where Dr. Reddy’s has started. It is also an area which is financially rewarding because world-wide and in this country also, the patient population is increasing every year. So this was a company which had no previous history of any discovery of drugs. It was started with a basically very ambitious programme that we are going to find a diabetes drug, because there are not many diabetes drugs. And the drugs that were in the market were also having some side-effect or the other. Dr. Reddy started this process at a time when he knew, in the early 90’s, that by 2005 or so, India would have to be an inventor other than an imitator. So by the time India signs the GATT agreement, we should have something in place. We are competing in the world market. We are not competing in India. In India, first of all, for a company like this which wants to make money, there is no big market to be very honest. Whatever you may say, companies have their own urge to make money. The cause of serving humankind is noble but the bottom line is money.

In the context of the research strategies in the area of diabetes, attempted by the firm, the respondent further elaborates,

More importantly what we do is, we would like to first understand what pathway is operative in the drug that has been discovered. Suppose this drug or molecule has some drawback. It does cure the disease but it also leads to some side-effects. Our intent here is, if I have to beat this drug, I have to now come up with a drug which would take care of the side-effect that this earlier drug causes. Right? So our understanding of the side-effect needs to be very clear. What is that causes the side-effect? The side effect may be, they lower your plasma glucose, but then they also make you gain weight, you also have some oedema, and you have water retention in the body. Still if there’s no other drug to address this problem, you say,
fine, so long as my sugar is controlled I don’t mind. But body weight also leads to heart related problems, and then you are getting into cardiovascular problems. This is a complex problem, your body fat is this high, your cholesterol is high, your heart gets clogged etc.

The therapeutic focus of the firm’s discovery research centre in Hyderabad has primarily been in the area of diabetes, while the focus of its unit in Atlanta in the United States has been in cardiovascular related problems. However, the firm’s research programs as a whole have focused on the following therapeutic areas: metabolic disorders, cardiovascular disorders, bacterial infections, inflammation and cancer.

The firm’s research laboratories are based in Hyderabad, India and Atlanta, Georgia, United States. It has employed a total of 283 scientists, including approximately 56 scientists who have Ph.D. degrees. The firm also claims to pursue an integrated research strategy with its laboratories in the United States focusing on discovery of new molecular targets and designing of screening assays to screen for promising lead molecules, followed by selection and optimization of lead molecules and further clinical development of those optimized leads in its laboratories in India. The motivation of the firm to establish a research facility in the United States has ostensibly been to have better access to research scientists in the United States and enhance its screening abilities for new molecular targets and access to high technology platforms.

Atlanta has been working on cardiovascular, we were working on diabetes. They have some access to medium throughput screening and all that, but they are in the U.S. so they can always outsource it. It’s our chemistry group that was making the molecules; those guys were actually taking some molecules from us. Its basically biology related work that they have been doing. They came up with two molecules in cardiovascular which have gone to Phase I. I don’t know whether they have gone through to Phase II. In that sense, I would say the R&D centre has been more productive here, but that’s also because the strength has been more here. There they have only about 25 people; here we have around 200 scientists.

94 Figures as of March 31, 2007
The firm’s strategy is essentially to come up with a drug, which is analogous or similar to an existing drug or class of drugs. This involves the modification of known compounds. This also means that the firm does not undertake research on a new family of drugs; rather it tries to find a new drug, within an existing family. However, coming up with improved versions of existing comparators also involves knowing the mechanism of action of the drug. The term mechanism of action may refer to a biochemical description at the subcellular or cellular level, or to a physiological description at the tissue or organ level. Understanding the mechanism of action involves an explanation of how a compound or a drug elicits a particular biological activity. A drug need not necessarily have a single mechanism of action, since these biological mechanisms exist at many levels, including subcellular, cellular, tissue, organ etc. The following remarks, also made by respondent 1 are an elaborate account of the every day processes and routines, the firm engages in, in its attempt to come up with these analogous molecules, possessing the requisite ‘attributes’.

The drug acts on different targets in the body. Targets are nothing but proteins. Now, molecular biology, cellular molecular biology in the last 50 years has given us an insight into how these proteins work their structures, etc. So we can have a drug which can modulate the function of a protein by entering the body and binding itself on the protein. That is the drug hits the target. The binding of the drug to the protein changes the protein’s activity or function. If you are designing the drug in such a way that it would bind at a place of the protein, protein you know is also a molecule, it would perhaps help the genes that are expressed by this protein, which causes, say for example, increase in sugar levels in the body. Through this drug they don’t increase, those genes may not be expressed. We are doing this at a genetic level. We are manipulating the proteins’ function. Protein is involved in expressing genes. Genes which are going to give rise to diabetes, give rise to high sugar level in the blood, high glucose level in the blood. So now the molecule goes and binds itself to this protein and alters its function so that it will not be able to express the genes for diabetes, which means that I have found a drug for diabetes. So then what I will do is I will carry out this experiment on animals like rat and mice. There are animals like rat and mice which can be made diabetic like humans. That means their sugar level is high, glucose level becomes high. So those animals can be bought from US
or you can raise them here. Put this drug into them and see, how much sugar you can decrease. That is how we do lot of experiments. We take this, put it in the animal, observe, and take out the blood to check the plasma. try to understand, discuss for hours together on what we do, how do we change the molecule and finally we are able get a molecule which lower glucose levels in the animals. Then we go to the higher animal. That means have safety studies on mice, rat and dogs. Put these animals on the drug for one week, two weeks, one month, four months, depends on the period specified. There are certain protocols – toxicology protocols that we need to observe. For example, you take this rat and put so many doses for two or three weeks and every two days you take out blood plasma and see how much sugar is there and there are protocols well defined, internationally accepted, this is not something that we have developed.

Using protocols or prior art, specified in medical literature, the scientists primarily attempt to establish how the drug acts in a target or specific locus. Pre-clinical research thus involves the extrapolation of data obtained in in-vitrio research to in-vivo animal tests. However, the problem with most compounds is that data obtained in most animal models are often poorly extrapolatable to human patients. This is what leads to the failure of compounds at the stage of clinical trials. Also, drugs elicit many pharmacological effects and biochemical effects and in many situations, it is unclear and uncertain, which specific properties of a drug play an essential role in providing clinical benefits.

About 90% of the discovery related activities carried out by the firm relate to known targets, which involve considerably less expertise and acumen compared to the remaining 10%, which relate to the discovery of new targets.

Organizing Research and Interdisciplinary Expertise

Pharmaceutical research involves different disciplines like chemistry, biology, pharmacology, toxicology, clinical science, chemical science etc. The firm has a total strength of around 300 scientists, from these different disciplines. The ratio of chemists to biologists is 2:1. Research is generally carried out in project mode and a typical fully
resourced project in the firm has around ten chemists and five biologists. Research personnel from other disciplines are also involved in the project, but the core project research team consists of chemists and biologists. The potential degree of success in a project is attributed to the level of expertise the firm possesses in these disciplines and successful communication among scientists belonging to these two disciplines. In this context, scientists with the ability to engage in team work, knowledge of these multiple disciplines and communication were perceived as invaluable to the success of projects. In this context, Respondent 3 emphatically asserted,

Pharmaceutical research involves different disciplines like chemistry, biology, toxicology, then you do the preclinical dosage, expertise in statistics, etc. so, so research that one tries to do is more or less driven by the expertise that one has within the company. So based on people's expertise and interest, we decide which people should be associated with which kinds of projects in which kind of therapeutic areas. This industry’s success is at the intersection of chemistry, biology, pharmacology, safety, clinical development etc and you’ll not find many individuals who will know all of these areas well; you need to have excellent team work to come to this common intersection. Another thing, speaking a common language, communication is very important, chemists they speak the language of molecules, biologists speak the language of biological processes, the pharmacologists they speak of what is the effect of molecules on chemistry and biology, the languages they use are completely different. In my opinion, success lies at the intersection of all this, bring all these people together; let them first of all harmonize the vocabulary they use or the vernacular they use. You need tremendous interdisciplinary effort here.

In this context, Respondent 2 added,

In addition we have statisticians; we have biochemists, formulation experts, it all this thought put together, coherently and moving ahead as a team that is involved.

Karlqvist’s (1999) and Brewer’s (1999) observations on the nature of interdisciplinarity can well be adapted in order to understand the dynamic of interdisciplinary research in the firm. As the above remarks illustrate, knowledge related to drug discovery lies at the intersection of different disciplines. The knowledge about new molecules, which have therapeutic value
and the pathways that these molecules assume in the body to treat the disease require not only an understanding of all the above-mentioned disciplines but also an understanding of how to connect this disciplinary knowledge. In this sense, the knowledge pertaining to drug discovery for the respondents thus constitutes a kind of meta knowledge. Respondent 1 (a medicinal chemist) also highlights the larger tensions and clashes inherent in interdisciplinarity, mostly between chemists and biologists. The respondent’s remarks are also perhaps indicative of the tendency with pharmaceutical scientists belonging to a particular discipline to represent themselves, their skills and their course of action as the most valid in an interdisciplinary context.

Certainly today, I tell you honestly, with respect to biologists, a medicinal chemist is much better equipped to do the research. The reason is when you brought down the understanding of biology to the molecular level, who will understand better tell me, why, because a chemist has appreciation and understanding of structure and function. When you talk about structure and function, you talk about molecules. Drug discovery is nothing but your appreciation of molecular structures, where you can appreciate molecular structures – whether it is protein or nucleic acid or small molecule. Of course biology will have a very important role to play in the post-genome era, mostly structural biologists, I would say, structural biologists are nothing but chemists. Structural biologists understand proteins, structure of proteins.

The reasons for these tensions are traced by the respondent to the very nature of the two disciplines and the history of specialization of scientific disciplines in general.

After all these centuries we have created disciplinary boundaries. You know what we did, we delayed our discoveries. 50 years ago, if the situation had been different, namely, if the chemists and biologists had worked like today, discoveries would have been started taking place during that time itself.

The respondent also provides an elaborate account of the disciplinary differences between chemistry and biology and the uncertainties inherent in the process of coming up with the analogous molecule.

There is a fundamental problem between chemistry and biology. Traditionally chemistry being a physical science, it is more exact, more of a data based discipline,
where quantification is done. Chemistry, being a physical science, is driven more by numbers and quantas. Whereas in Biology still...lot of things are a black box...what goes on in an animal we don’t know. A chemist is a physical scientist. A physical scientist requires exactness, numbers, and calculations. Biologist is dealing more with enzymes, things at a molecular level. Body is a highly complex jungle of proteins and processes. We only extrapolate a lot of things. In some cases, it’s very clear, you put a drug in an animal, something will happen and we know that. It’s fine so long as you have a reason for your assumptions. But all this changes as things become more complex, as you change a drug... Now you have no guarantee that the new molecule you are trying to would be working by the same rule, you cannot be very sure. That it is going through the same path way. It might be one of the pathways, but at the same time it is also going to do something else. So the biological system is a highly complex system. Why it is a complex system is because unlike the chemical system where say 25 laws of physics and chemistry are operative, the biological system is a multi-component system. There are so many variables, so many chemicals. To get any information out of this complex jungle, go to this very defined landscape of chemistry. You know the sequence is different scientifically. A lot of these biological things are extrapolation. But in the absence of any well defined, quantifiable, verifiable thing you only accept it. Because you really do not have an exact yardstick, except that you are looking for some output. Output in the form of a logical response, output also in the form of some chemicals that are released in the body that are manipulated or calculated. These can be measured by simply taking out the animals gut and there are machines which can tell you that. But those are at a very superficial level, because after all how they are produced, what pathways have been followed in producing them in the body, you can only guess at. You can only say, for instance, the sugar level has come down to so much.

These above-mentioned remarks highlight the dilemmas and problems of pharmaceutical research, which are common to all researchers in industrial laboratories, in India or in the West. While on the one hand, the attributes of the molecule, in terms of parameters such as potency, safety and efficacy, are ascribed in quantifiable terms, most of the processes in the human body, which is perceived as ‘a complex jungle of proteins and processes’ are still an unknown quantity for the scientists. This renders the prediction of adverse or therapeutic effects of the drug extremely difficult.

There is a historical angle to this remark, which perhaps needs to be elaborated upon here. India has traditionally been perceived to have excellent skills in chemistry, which were honed in the industry in the period prior to the patent regime. The contribution of biology to pharmaceutical R&D has been relatively less, as patented drugs could be copied through a
different process and these essentially required good skills in chemistry and did not really require any great knowledge of biology. Again, there was no collaborative history or ambience of drug discovery related activities in India unlike the West, till the mid-nineties when the impending patent regime resulted in firms slowly making a foray into discovery related activities. Biology as a discipline flourished largely in academia in the pre-patent regime.

The need to transition from being ‘copy cats’ to ‘inventors’ also resulted in firms grappling with problems relating to interdisciplinarity, expertise in different disciplines like chemistry, biology, pharmacology, clinical sciences, not to mention ‘cutting edge’ disciplines like bioinformatics, genomics and proteomics. An interesting aside is that the firm’s strategy to come up with analogues is common to the discovery related strategies deployed by most Indian firms, and even a few Western firms, the difference being that the present firm was somewhat of a pioneer in this endeavour. The attempt to come up with analogues is also the outcome of Indian firms’ efforts to take out quick patents and cash in on their well-honed skills in chemistry.

Still, problems related to these basic disciplinary differences and unpredictability involved in finding therapeutically beneficial candidate drugs, are for the most part, couched in terms of norms relating to the ‘challenging nature of the pharmaceutical discovery enterprise’, the level of capabilities required ‘even’ in analogue research and the logistics of interdisciplinary team management. Reference is also made to the common ‘jargons’ that have evolved in facilitating communication between these two disciplines and which are

95 The respondents’ reflections on the firm’s expertise in this area have been dealt with a little later in the chapter
helpful in overcoming the fragmentation of knowledge related to drug making. In this context, Respondent 1 mentions,

There is a common jargon that has been evolved. Well after all, the art of drug discovery is not new, I mean it is going on for the last 40-50 years, adjustments, evolution of certain common vocabulary, you know terms like efficacy, potency, half life, pharmacokinetics, pharmacodynamics, pharmacokinetics is a word that exemplifies the input of drug in the body, and how it reaches the target, target is that protein which is causing the disease, you want to disrupt its function so that the disease is not caused. So your drug has to be made in such a way that it reaches there. Body is a big jungle, you either inject it or take it in the form of a pill, but body has so many barriers, you have gut, you have intestine, you can see the kind of complexity that body presents to the drug, you are hoping that it will hit the target, its that kind of complexity.

In this context, the respondent also makes a reference to the ‘progress’ achieved by these disciplines, which have facilitated the attainment of a common ground to discover new drugs. In this regard, respondent 1 elaborates,

What has happened is that in the last 3 or 4 decades, enormous progress in biology has taken place, biology earlier was more of a phenomena of physiological response, looking at the entire thing in a macroscopic way, pain, temperature..it was more of a physiological parameter that you were measuring, so a chemist who is making a drug, he can give a drug to you as a biologist and you will tell the chemist, if it is working or not, perhaps that might have been the only conversation between them initially, such basic thing.

The common ground for communication between chemists and biologists is also attributed to a shift in the engagements of biologists from macroscopic processes to microscopic processes operating at the molecular level. The discovery of therapeutic substances and a greater understanding of bodily processes are attributed to this shift.

The developments in modern biology, which were translated from a more macroscopic understanding of biology to microscopic or a molecular level. Biology has undergone a tremendous change in its entire existence in the last 100 years or more, one started understanding biology or anatomy or what ever you call it at a molecular level. When you are talking about molecular level, you are talking about chemistry. That’s why molecular biology comes into the picture, earlier you had developmental biology. We had nothing to do with the molecule, now molecular biology has brought the two disciplines together. The biologist knows how to work with cells and tissues and all that, how to develop cultures, and also how to give a chemical basis for this research. When you talk about protein, DNA, Nucleic acid, glycoproteins, glycolipids, fats, all this is chemistry, chemical substances, when
biologists started talking like this chemists started appreciating. Yes, cell is composed of phospholipids, inside that there are layers, inside that there is nucleic acid, nucleus has proteins, other small molecules, every thing was sort of splitted into chemistry, now that understanding led the common ground for the two to come together. And that is why you see in the last 20 years or less rapid advance in our understanding and discovery of molecules... Earlier it was only a black-box. Earlier what happened, people made one drug in large quantities and then they went on trying on all animals, one drug was tried for cancer, hypertension, diabetes and for every thing. Because they did not understand. A particular drug may cure or act as good sugar lowering agent or as an anticancer or as hypertension. So people didn’t understand much. Today that understanding is becoming clear. Today, because biology has been brought down to the level of molecular biology, biochemistry, the biological principles are understood by the biology guy, the chemical related are understood by the chemist. The moment of all these things happened, the synergy between the two disciplines started. So then common jargons came about, were accepted by both sciences and all these collaborative efforts began to happen.

This elaborate historical account by respondent 1, of the shifts in the preoccupations of biologists and their collaborative efforts with chemists, is also indicative of the body of scientific beliefs and principles anchoring their research enterprise. The respondent also highlighted how these collaborative efforts have led to the gradual development of common engagement and shared meanings with respect to attributes like ‘potency’, ‘efficacy’, ‘toxicity’ etc and also the emergence of disciplines like medicinal chemistry. Medicinal chemistry is generally regarded as a discipline that emerged outside the ambit of universities and within the pharmaceutical industrial enterprise in the West.

See, earlier for chemists, potency was not a cause for concern, because if you are not working in medicinal chemistry you are not talking about potency...you work with a biologist to discover drugs then you start talking about potency. And all that related stuff about...otherwise typically, as a chemist, I make my molecule, I write my paper, I’m working on a non-medicinal theory, why should I worry about potency, its only when you start working on a drug then you start worrying about potency, efficacy, toxicity.

One of the strategies deployed by the firm to operationalize this interdisciplinary related logistics includes placing the scientists involved in a project in physical proximity
and encouraging them to have periodic and frequent formalized and informal discussions. In this context, respondent 3 mentioned,

Put them all together physically, we make sure they are all on the same wavelength, the chemists, biologists, statisticians, pharmacologists, clinicians, the way we do that is, we build teams around a project, and the teams and projects comprise people from each of these disciplines.

Decisions on the nature of projects to be undertaken, involving specific approaches and methods to discover new drugs within each of the therapeutic areas being researched are undertaken by management committees in the firm. The scientists in these committees possess expertise in a wide variety of disciplines, ranging from chemistry, pharmacology and toxicology to clinical development and chemical science. Also, these projects are designed keeping in mind the objective of targeting therapeutic compounds, which are efficacious in a large percentage of the population. In this context, respondent 3 stated,

We have management committees, comprising of senior leaders, individuals in this company who have expertise in multiple disciplines. My boss is a physician but he does drug discovery, myself, I have spent almost 30 years from the late seventies till today, I’ve been at the forefront of biotechnology, in fact I have pushed the envelope all the time, so I necessarily have to be familiar with biology, chemistry, maths, physics, computer science. The management committee sits out and discusses each of these projects, what are its merits, what kinds of priorities we need to assign, what kinds of people need to be on the project, besides this we also have commercialization people, who give us inputs as to whether this is a valuable project or not, at the end of it we are not doing science for the sake of doing science, we doing science for the sake of humanity for the sake of society. And we have to make sure that we are targeting the largest or the maximum number of people that we can target, not just because of the business factor but driven by unmet medical needs.

The management committees in the firm clearly shape the research agendas, rather than individual scientists, though they may place project proposals for consideration and approval by these committees. Respondent 1 elaborated further on the criteria deployed for selection of projects.

The team would place this (ideas) before the senior management, we 3-4 seniors, we would discuss it, suppose they have a project, they would write it down and then
propose it to us, we look into it and then give a nod to it, okay guys go ahead, they will make a project like what is good, what is there in the market, how much money it will cost, how much manpower, we (the committee) belong to different disciplines like chemistry, biology, chemical development, we have a development guy because ultimately we have to develop the molecule right, for human and clinical trials, so we will look into it, read it properly. In a science based thing, four people cannot differ so much, they may have their own reservations about whether the drug is going to be successful, whether the approach is going to be good, whether its going to compete with the existing drugs, whether it is going to have better properties, all those questions, reservations are generally expressed, there is no doubt about it, we sometimes send back the project, ask them to come up with a better one, see objections that could be raised are number one, is it a worthwhile project, whether what you are doing is going to beat the existing drug in the market, whether the science that you are going to do is going to enable you to beat that drug. Methodology is what we look at, that is, science part is good, but how are you going to achieve it. Feasibility of the project, manpower, costs etc. Obviously the committee consists of seniors, people who have experience; we go through scientific as well as non-scientific aspects of it.

The criteria for selection of the projects are a combination of factors such as commercial worth, financial and technical feasibility and the potential in terms of early clinical development and commercialization. Both strategic and operant autonomy (Bailyn 1985) largely vests with the management, though scientists are provided with the space to initiate research projects, within the broad therapeutic mandate decided by the management. The ability to generate quick, rational, established evidence and reliable data, suitable sub-populations for clinical trials, suitable technologies for commercialization, and the patent related space to explore within the classes of molecules in the scaffolding of the comparator drug, constituted important criteria for the approval of projects.

The practices and the every day routines involved in the generation of facts pertaining to the candidate drug are elaborated upon by respondent 1 with the following remarks.

As this team works, this team has to understand what is the disease, the disease process, how much is known about it already, how many drugs are there in the market, what are they, have they any side-effects, this is the job of the team. The team then periodically meets and discusses, the chemistry fellow comes up with the
molecule, and the biologist has to take it to the animals. One of the things that would come up would be, hey, you are going to design the molecule this way, but it doesn’t look like to me it will have any probability in terms of intellectual property. So he will check with the intellectual property guys, we have a separate department here. Then he would say, this is a patentable molecule I am going to make. Patent is not an issue. Then some one will say scientifically what problems you will face? What are the results going to be?

In each molecule there are certain things, there are costs of the molecule you’re making, whether it is easy or not, because you don’t want to end up in making a molecule which is going to take 3 or 4 months. And cost wise it may be more, then why do you want to make it? Time is a major factor here costing you very much. So these are the issues. Scientifically sometimes, the science that he is using to make those molecules, the kind of chemistry that he is going to design sometimes he may be questioned on that. But those are very common things. Those are nothing great. Then he would have his own reasons to string it together.

The time taken to come up with the molecule, the costs involved, the ability to maneuver within the space of the patent of the comparator molecule, these are some of the issues, which the chemists in the team have to contend with.

Discovery research at the firm level is generally referred to as pre-clinical testing, involving test-tube level experiments and experiments with animal models. The ‘qualification’ of a drug in the pre-clinical stage generally involves investing it with quantifiable attributes, relating to its distribution and absorption, safety, potency, efficacy and toxicity. These attributes are formulated using existing comparator drugs in the market or available literature in the absence of existing comparators as benchmarks. Theoretically, the attempt is to arrive at a drug, which is a better version of the comparator in terms of side effects, though it may not always be possible in practice.

The medicinal chemist makes the drug, biology guy would take his own screening test, which we call as the in-vitro test, which is basically a kind of test tube kind of test and he would short list the kind of drugs to be put into the animal, because we can’t put every kind of drug in the animal, because animals are not so easily available, so some drugs would show nice results in animals, so they would periodically meet, they would say oh this drug looks good, however this drug is not getting distributed properly, so they would try to make some changes on this, so that the drug gets absorbed or distributed properly. Because for a drug to be effective, it has to be distributed or absorbed properly in the body. See there are 4 things that we
call ADME, Absorption, Metabolism, Distribution and Excretion, there are the four principles governing drugs made or subjected to animal experimentation or human experimentation. What we do is that we address these four parameters. If any of these parameters are not being addressed properly, it’s not a good drug. And what we do is based on the experience, based on the market, based on the research, based on other drugs and generally a good drug must be something that is distributed well, something that is absorbed. What we do normally is in the literature you have some ideal drugs, so you say this is my yardstick but you only rate with respect to that, you don’t try to achieve those kind of things, I mean, so they provide us with some benchmarks, and the drug which is there in the market, they provide us with some benchmarks, you always compare your new drug with the drug which is existing in the market. So whatever ADME property is there, you take that.

On the issue of how a typical project was conceived in the organization, the respondent put it in the following way.

Two people get together, let’s say, two senior level people, one chemist and one biologist, they’ll say because this company is doing diabetes, let’s find out some other ways of making a diabetic drug. They will obviously read, discuss, and we have provided this opportunity, that anybody, any group or individual can make a proposal and then the management looks into it, provided of course we have the resources, of course we can’t take up every project, we might tell them, you can do this project, let’s say in diabetes or in cardiovascular, what happens is that prior to this they will form a team, they will make a proposal and they will circulate it to us.

The explanations for the resolution of issues and consensus in an interdisciplinary context, during the course of team work on different projects in the firm, are again couched in a broad discourse of the ‘objective’ and ‘factual’ nature of experiments and data generated by the team and the privileging of the scientific method as compared to the methods used in social science disciplines. However, this is tempered with the observation that science may also involve assumptions and different ways of interpreting results to some extent. As respondent 1 states,

The question of how consensus results during our work on different projects, you see, when two people work together, they have to understand. Science is not like history or geography. Science is black and white, it is data driven. If a chemist does not agree with a biologist, it’s only up to a certain point. Sometimes a scientific experiment you do has a certain result and you interpret the result in a certain ways. There are often times when scientific results could be interpreted in different ways depending on your way of looking at things. At some point of time, however, when
you start looking at things in black and white, the data, it’s very clear, there is no question of dispute, you simply have to accept. You have to understand, one good thing about science is that, though it is not a perfect discipline, there are a lot of assumptions in science also, to be very honest, but those assumptions are within certain limits, so that, you are not badly off. The whole practice of science is driven by this. May be at the initial stages, the biologist and chemist may have certain tensions, because either you don’t believe in that hypothesis or dogma or you have not understood it properly. Two things can happen. You say no, no my thinking is that this thing should go this way. But then ultimately, whatever you say, whatever practices say, ultimately experiment decides. You do an experiment; you see what happens, black and white. You see the results.

The motivation and anxiety to have an everyday hands-on involvement with the intricacies of particular projects and to understand the terminology used by scientists belonging to other disciplines is articulated by respondent 1 in terms of his professional responsibilities, the ethos of ‘innovation’, which demands a fuller investigation into its processes, the motivation to succeed in the research enterprise and also in terms of his position as spokesperson for the firm’s innovative achievements.

As a scientist you don’t think that way. As a scientist in a drug discovery company like this, what is your main motto is going to be? Your main motto is that I want to discover, I am going to make a drug, I want to do whatever is required in the process of doing it. It is not that you think, why should I do so much? That guy is already doing, I will do a little, and the rest is his job. No. If you do like that, I think you will never discover. Somewhere down the line, you would have this whole operation flapping. If you want to be an inventor or co-inventor of something, you want to understand the whole thing in the right spirit and depth of it. Why do you think you need to understand that? It is for your own good. Tomorrow I invent a drug, come and tell you and the outside world and I would not even know the whole thing about it, I would feel very uncomfortable, talking about it. If somebody asks me a question, regarding which aspect of this drug I have contributed to, and if I can tell more than or outside my discipline, I will be a kind of a true inventor of the drug and I will also know in great detail about the entire process of this discovery, of which I am a part. As a scientist, it is very important for you, especially when you are doing something of this nature where you have to work with people with different skills, different backgrounds, where you have to meet them every day, discuss, it is very important for you to at least sensitize yourself, if not completely, at least part of that discipline. There are jargons; there are languages in those disciplines which you have to use when you are talking to them. If you cannot pick up that jargon, you cannot talk; he cannot come and tell you anything.
Conflicts in the research process are articulated in terms of tensions arising from credit sharing.

Division of labour is a cause for dispute; conflict is still there in many places. You know this tendency to think I did more and my contribution was more.

The potential of the drug to be efficacious in a wide population, available scientific expertise and commercial feasibility are primary considerations, taken into account, whenever differences of opinion arise with respect to two candidate molecules, which exhibit therapeutic potential. As respondent 3 put it,

First it has to have an unmet medical need criteria, a wide reach, there are lot of molecules which may have an unmet medical need, but the reach may not be there, so we have to look at the reach also, thirdly what’s the science behind it, what kind of science has been already done and if nothing has been done then how feasible it is, then what patent landscape we are trying to, and we have to make sure it is technically feasible also. There will always be debate among people as to targets, oh maybe this target is better or that target is better, that’s a healthy debate, we encourage those debates and don’t shy away from it. Also, based on our research capacities we make such judgement calls, it’s possible that we may miss out on a good opportunity, but we want to ensure that what we do has a good probability of success.

Again, the discovery of analogous molecules, with a known mechanism of action, is visualized by the firm, as a research strategy with greater chances of success and a relatively less risky venture, in comparison to discovering a new family of molecules, where the mechanism of action of the drug has not been determined. In this context, Respondent 3 also elaborates on the intense competition among firms working on a similar category of molecules.

Analogue research is one area where you are not likely to fail; if you are going for unprecedented and novel mechanism where the proof of concept is not there, then chances of becoming success are 50:50 or even zero. But when you take a precedented mechanism and if there is the IP space and the possibility to have a better drug, in terms of safety, in terms of pharmacokinetics, then there is a possibility to succeed. So that is one approach fundamentally, where most companies emulate that as fast follow-up. However, if somebody is working on X
project, then immediately all over the world, since the target has been identified and it has got a liability to succeed, a drug like molecule can come out, so everybody will start working on it..

The capacity to head research teams in the organization is articulated in terms of adequate experience in the industry and know-how related to multiple disciplines rather than in terms of a particular kind of specialization. Respondent 3 elaborates,

We look for people with some experience in the industry as team leader. I will not put a PhD, with no experience of industry as a team leader, at least a person should have 4-7 years of experience, who knows some biology, some chemistry, something about the disease area and those are the kind of people I would pick as leaders and let them basically run the show. They could be biologists, chemists, pharmacologists, physicians, for all I care, as long as the capabilities are there, the skill sets are there.

Also with respect to the firm’s capabilities and criteria for hiring expertise in molecular biology, capabilities, which are generally perceived as being in short supply in the pharmaceutical industry in India, respondent 3 articulated how quality of publications was seen as the predominant criteria and that the firm had recruited a team of biologists from all over India and abroad.

We have a lot of people who have done their PhDs and post-docs in Europe and America; we’re pretty excited about the fact and we examine the quality of their publications, what they have done in the past, what they are doing currently, and I think we can make a fairly good judgement of how much molecular biology they know. So it’s not a rocket science, its just a question of putting in some diligence, some time to look at their CV, may be even ask them some queries about what they are doing, it shouldn’t be difficult to figure out how good they are. We are not going to stop short, look at geographical preferences or locations, and we scout for the best brains from wherever they are.

New entrants, especially those with a predominantly academic background, are trained by senior personnel in the intricacies of industry-driven research. The criteria for inducting personnel at the senior or the management level was essentially their experience in the industry, particularly in multi-national pharmaceutical firms, to ‘leverage’ the know-how
and expertise acquired from these firms, in addition to expertise in the therapeutic mandate of the present firm.

The assumption that most of them are from academics is not completely correct. We have people here who have many years of industrial experience, first of all, within this company and also in the pharmaceutical industry. Our President, he comes with 10-15 years of experience in multi-national pharma, I also come with almost 15 years of experience in multinational pharma, we have several people with those kind of experiences and we look for people who have that kind of experience in the industry. We use these people’s knowledge and skills and we try to train the new entrants. We let them (the new entrants) shadow people, we train them under these senior people, as time goes on they get trained.

In this context, Respondent 1 also highlights how the firm strategically blends the competencies of recruits from academia and industry in attempting to ensure success in its projects. It also regards this blend as an essential part of organization building. Recruits from academia, especially from abroad are prized for their abilities to bring in new ideas and these ideas are leveraged for initiating new projects, while recruits with experience in industry are valued for their execution related capabilities, ‘practical’ approach to handling the problem of discovering candidates molecules quickly and therefore utilized more in a context of meeting project deadlines. The following remarks are indicative of how the firm constructs research capabilities in academia and industry in the terrain of pharmaceuticals. The firm’s discourse, in relation to making its scientists work in therapeutic areas, which are potentially lucrative and mandated by the management, is also couched in terms of its anxieties in being answerable to its investors and shareholders.

We have people from Harvard, Stanford, Oxford, IICT and University of Hyderabad. They have excellent labs in the US, from where lots of these scientists have come. Quite a few of them have come from industry also, from abroad. So, when we hire people, we normally look for this kind of blend. For example, where we have a project in which things are more or less in a state where we have deadlines to meet. So, a guy who has been in industry perhaps will do this job better. Since, he or she is used to it. Now, I will not put a guy who has been in academics or who has no prior experience of working in industry here. I would rather put him or her in a project during the initiation stage. While initiating a
project, you need to have ideas; you can afford to use your creative skills and knowledge in this way. So, I think this guy who did not have any prior experience of working in industry, a fresh postdoc, let’s say, is suited for that job. This is basically for building the organization. You have to define their boundary conditions and set them free. Boundary conditions like, you can’t just go and do anything. The company has its own mandate that you should work in cardiovascular or cancer or in diabetes but anything within that, which has the likelihood of a prospective drug. Industry has a mandate, industry is using public money. They have to justify why they are spending. Our’s is a public limited company, we have to justify to investors, the public.

The articulations of Respondent 2 were also in a similar vein. In addition, the respondent also highlighted the importance of a long term commitment to ongoing projects by the management, in a situation where results were not immediately forthcoming or favourable. All of the above remarks also highlight the different sets of values and expectations associated with scientists from different disciplines and academic and industrial expertise. In attempting to have a merge of academic and industrial expertise to bolster the success rates of ongoing projects, the firm essentially attempts to emulate strategies followed in countries like the United States.

A little patience is also required from the management, because it could happen in one year, it could happen in three years, but one has to have a time frame, okay, we will work for 5 years in this field and these are the targets we will pursue. Along with the industry people, some of the people who are working at different levels at the bench in the firm come from different premier institutes in India and abroad, with pharma background, so it is a merge, and if you look at the US, they have a tie-up with the universities for developing and same is the case here, and here also we are applying the same skill tools, industry oriented leaders along with the people coming with post-docs, moulding themselves to whatever projects we have, towards our objectives in drug discovery.

The interviews with respondents from other firms had also highlighted the increasing attrition rate of scientists in these firms. In the context of the strategies deployed by the present firm to retain its employees, respondent 3 stated,

We keep our eyes and ears open, we keep our networks alive, there are a lot of people that we have worked with in our past jobs, we have friends, enemies, we tap into all sources, so we always keep a healthy pipeline of human resources also. We
try to create the best environment that is potentially possible and once we have that, people normally think two times before they leave this place, because the fear of the unknown is far greater than the fear of the known, one of the things we do is nurturing people, training them, we do it with feeling, with compassion.

In the context of the strategies used by the firm to avoid intellectual property violations by its employees, the respondent added,

Patent is in the name of the inventor but the rights are made out in the name of the firm.

Respondent 2 remarked,

We have a legal agreement that employees sign, that they can’t use the same scaffold, the same area, keep away from the targets that he (the employee) has been working on here for some years, it’s all built in, so the legal document that the employee signs cover a lot of these issues.

The firm resorts to formal legal agreements to avoid violations of confidentiality on the part of its employees. Norms pertaining to breaching of intellectual property related protocols, professional integrity and credibility within the small community of discovery related researchers are invoked in the context of the increasing managerial control of the knowledge generated by the researchers in the firm. Clear demarcations are sought to be established between ‘generic’ and ‘proprietary’ information. Here, respondent 3 stated,

I have in the past worked for two reputed MNCs, the first and sixth companies in the world, and my reputation is always at stake, if I would have left my first MNC and gone to the second MNC and told them what I worked on over there, two things would have happened, my credibility with the second MNC would have gone down and second they would have fired me immediately since they would get liable for that. Since I would have used the first MNCs’ know-how. But besides that I have a future and a passion to do science. So if I violated these ethics, a third firm would not even take me at work, so where’s my career? Besides, you must understand that in the pharmaceutical industry, whether it’s at the global level or in our country, most of the people know each other. It’s a small community, and once your reputation is tarnished in that way, it stays tarnished. Even if I were to leave my company, which I won’t, but let’s say I do, I’m not going to go and talk to the other company about what I was doing here. I don’t talk here about what I did in the past,
since I have to worry about my reputation. I have to live up to my people, network and scientific community also.

There are certain generic technologies or certain generic experiments or generic know-how that you can use anywhere, for instance if I want to use a particular genomic sequence or sequence a particular gene, I can buy a machine and do it, that is not proprietary know-how but if I have a gene and I say is this particular protein a class of proteins like say kinase, there are tests available to tell me whether it is kinase or not, those are generic information, but what does that kinase do in a particular situation or whether it has been manipulated in animal models or humans, that is proprietary information. That I cannot disclose, but if I say it’s a kinase, hey the whole world knows it’s a kinase, so what? And so you have to distinguish between what is generic and what is proprietary information. Even if you have some proprietary knowledge and it is published, then it comes in the public domain, I can share that information with any company because it’s public knowledge.

In response to the issue of how job switching occurred as a team, respondent 2 added,

The Indian conditions and system is different, see when a senior scientist goes, sometimes he would like to take his manpower with him and establish it at a different location. I don’t think its happening now or it will happen in the future, now the industry has begun to mature in that sense and it also has more opportunities.

The new patent regime has created difficulties for the firm in terms of being able to forage for potential candidates since multinational companies have resorted to patenting an entire family of molecules within a therapeutic category and ‘ever greening’ or extending the life span of patents on existing drugs by modifying and presenting it as a new drug or discovering new indications or new dosage forms for it. The articulations here are in terms of how the acumen and expertise of the scientists are deployed to work around these issues. As respondent 3, put it,

It’s creating a layer of difficulties, you don’t have to breach it (patent), you just have to work around it and that’s where your skill and intelligence comes into the picture, that’s where the human being becomes indispensable.

While the firm is confident about its know-how in terms of being able to come up with new processes, having honed these skills in the period prior to the product patent
regime, the necessity to manage novelty and costs of producing the drug is a major source of anxiety. The discovery of new targets is viewed both as a risky and potentially lucrative venture since a successful drug would fetch huge returns.

In process R&D for instance, in the case of some molecules which were having a specific process, we have overcome the obstacles, there are always ways and means, earlier we could make a change in the process, and have non-infringing process basically, sell it and get a profit, with the drugs available in the West. Now in the new patent regime, it’s difficult but very possible and we are doing it. And we have to think of the costs, and then the drug has to be sold at a nominal cost. But when it’s a question of new targets and the target has got something vital, then the question is a little difficult, but there are ways and it’s not impossible. The advantage is that if you discover a drug and put it in the market, you can decide the price.

In the process, the firm has also deployed aggressive strategies in terms of Para IV filings or challenging existing patents of multinational companies, perceived as an essentially “high-risk, high-return” strategy. In the context of how the firm actually made risk-benefit evaluations, the articulations were more in the form of generalized explanations of the uncertainties involved and what factors were considered prior to venturing into litigation. As respondent 3 remarked,

Litigation involves a whole lot of factors like company strategy, it’s a business strategy actually, your legal strength, position on the patent, how good your claims are, the ball game is once you get into litigation, trying to extend it claim by claim with legal language, things like that, what are the comparators, what competing patents have been filed, it also depends on factors like where the case is going to be tried, even geographical locations can make a difference, so it’s very difficult to make a comment as to what the outcome of a particular litigation can be. We have a very good IPR division. They are basically scientists, could be chemists, biologists, pharmacologists, but can also mould themselves to thinking from the legal angle, basically with patent law specializations, they take training, attend meetings and acquire basic knowledge as to how to interpret, our capabilities here are slowly emerging.

These legal strategies have not really succeeded, with the firm losing one case against Pfizer and other cases still pending in the courts. The reasons for venturing into the

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96 See Chaturvedi et al 2007
discovery of analogous molecules was also articulated in terms of standard explanations about the significantly lower costs of discovery research activities in India due to the lower levels of R&D related salaries, skills in chemistry, availability of infrastructure and the ability to adhere to Western manufacturing protocols.

The cost of discovering a drug in India is about one-fourth of the costs in the West. About one-fourth of eight hundred or nine hundred million, which is the cost for discovering a drug in the West. With the same quality, for various reasons. One reason is the R&D salaries and other wages are not as high as in the West. Secondly, we have the infrastructure, we have excellent skills in chemistry, the capabilities, India happens to be the fourth largest manufacturer of bulk chemicals and drugs in the world and we have the maximum number of US-FDA approved manufacturing units outside the United States and that itself speaks about our capabilities, our chemists have a way of cracking the process of the known innovator and coming up with a different process but with the same quality and pharmacopoeia requirements.

With respect to outreach activities, or participation in conferences and seminars, Respondent 1 claimed,

We go to top level science congresses. Where really serious science is discussed, business is discussed you want to go there. See there are some very major conferences in the area where in which we work. So, these conferences are held by it world-wide, every year. These are American Diabetic Association and American Heart Association; these are two big conferences, where people from all over the world come. And people from different disciplines come. You know scientists, biologists, doctors, clinicians, clinical development biologists, anybody. That is the beauty you know! People, leaders from different areas come and they give talks. There are talks from some labs on some new results. Then, there are talks about the future, what we should do. So these are the conferences where we can learn a lot.

The use of automation and software-guided technology has been relatively less prevalent in pharmaceutical firms in India, except in the case of some multi-national companies like Astra Zeneca and Nicholas Piramal. Drug discovery strategies in general are of several types. They may involved empirical or trial and error methods, involving the use of machines like high-through put or medium throughput for determining therapeutic activities in compounds. In the process of such screening, some compounds or drugs are
found empirically to exhibit some therapeutic activity, and a search is then mounted to
determine their mechanism of action. In some other situations, biological mechanisms,
including mechanisms like enzyme stimulation, receptor inhibition, biochemical changes
etc, are used as targets in animal test models. Newly made chemicals are evaluated in these
tests for their activity. This kind of discovery research is largely carried out by firms in the
West.

Drug discovery techniques in India usually follow the method of rational drug
design. Instead of using random screening procedures, especially with known mechanism of
action and targets, the structure-activity relationships involving the correlation of observed
biological effects and the structures of the synthesized compound or candidate drug are
carried out. This may be done through manual techniques or sophisticated technology,
depending upon the financial resources and capacities of the firm. This also involves using
some selectivity and judgement in terms of which compounds to synthesize. Some of the
issues involved here, involving debates among the chemists and the biologists pertain to, the
reproducibility of the biological data, which is obtained in the laboratory, the physiological
significance of the specific biological effects measured in animals, the clinical implications
of the biological effects observed in the animal model etc. Serendipity or the luck factor
also plays a huge role in the discovery of a new drug or new indications for an existing drug.

The respondents were largely disdainful about the hype and projections surrounding
the use of sophisticated and automated techniques in the laboratory, since, according to them
these techniques have raised the cost of research tremendously in the West, but have failed
to provide the projected quick-fix solution in terms of an increasing number of blockbuster
molecules. As respondent 1 remarks,
Today also this firm is going in the same way, a little more we can afford, in terms of technology, but not High Through-put and things like that. In the nineties, companies in the West began spending on High Through-put, accumulating huge libraries of molecules, but now more than 15 years down the line, what have they done? Where’s the drug? So it’s not as if by buying big machines, by automating, you can innovate, especially in drug discovery. The pipelines of pharmaceutical firms are drying; they need to come up with new molecules quickly. In India, we are driven more by idea-based research. In the Western context, research is more driven by technology. These moves towards automation, software-guided technology in the West, have not really worked. No matter how smart the computer-driven technology, you are working with, ultimately it’s driven by ideas; you need to use your mind.

The respondent’s remarks are also indicative of the image of itself that the firm attempts to represent, how it positions itself, as a firm driven by the ‘ideas’, ‘skills’, ‘indigenous know-how’ and ‘acumen’ of its scientists in contrast to the ‘technology-driven’ Western pharmaceutical firm, in the intensely competitive terrain of drug discovery. Such constructions are also evident in media representations of the ‘successful’ entry of Indian pharmaceutical firms in the international drug discovery scene. In this context, the respondent elaborates,

That’s because high-throughput is a very costly technology, Reddy’s, right from the beginning, have used indigenous ways, there’s not that much money that they have spent. Indians, if you see, by nature, are very creative beings and very hard working. Today we may rely more on technology. But I think this tradition of thinking on our fingers, of creativity and hard work is responsible for our rise. At the time we started drug discovery, we had very good chemists. You know, traditionally, India has been very strong in chemistry. And we started with that and we did have some amount of success.

These views are echoed by respondent 3 and respondent 2. Further, both these respondents also elaborate on the kinds of technology that the firm has begun to use in the recent past. The managerial level experiences of its senior scientists in multinational companies in the West also dictate the firm’s strategic decisions about a relatively modest level of investment with regard to the technology used in drug discovery techniques and the
emphasis on the creative acumen and expertise of its scientists rather than sole dependence on technology. Respondent 3 remarks,

We use Structure-Guided drug design (SGDD), many people use Molecular Mechanics drug discovery (MMDD) also, these are all various terminology, but especially I love to use the term computational chemistry, I think that it is a catch-all for all this. Historically, and this is where your experience and knowledge counts, we have come from big pharma, both my boss and myself, and we noticed that HTP was a fashion in the mid-nineties and early 2000. From our experience, we have noticed that HTP screening has not been as successful as has been touted. We are not in favour of HTP screening because we don’t want to go after random molecules; we haven’t seen that success anyway, so Medium Through-put is probably one of the ways to do screening. We do MTP and low through-put screening. Low throughput is just manual screening, medium through-put is also manual to some extent and you can also have machines to do it..

Respondent 2, in addition, describes the problems associated with combinatorial chemistry, in terms of reducing the purity levels of the compounds generated through the technology. He also highlights how the failure of Western firms to achieve success in terms of successful drug candidates has driven them back towards semi-automated technologies, with research strategies, similar to Indian firms.

It will be 95% in combinatorial chemistry in the initial stages since you are just changing the initial bio-modifications, I’m not an expert, but I know the fundamentals. Also, HTP has given you an avenue to screen large libraries of molecules but they have not fetched results, so they are also back to semi-automated technology etc.

These observations, especially those pertaining to the limitations and failure of automated technologies in terms of fetching required results, have been borne out to some extent in empirical studies of the pharmaceutical industry in the West. Moreover, the last two decades have witnessed that most of the ‘new’ molecules discovered by Western pharmaceutical firms have been also been ‘me-too’ molecules rather than ‘de novo’ candidates based on a new family of molecules.
With respect to ‘cutting edge’ disciplines like genomics and proteomics, their use was confined to the understanding of the mechanism of action of the comparator drug or basic toxicity or safety issues. The respondents’ remarks indicated that the firm was in the process of building its capabilities in these technologies. The use of bioinformatics in its discovery centre in Hyderabad, was again confined to its use for analogue research rather than the examination of new targets, which was carried out in Atlanta.

Not that much, to be very honest. Not many companies here do that, because it is still in the stage of infancy. I will typically use bioinformatics, if I have a programme where I want to know new target proteins. That we don’t really do much here. We are not actually in the game of looking for new proteins all the time. There are biologist colleagues at Atlanta, they try to look for it there, that is why we have opened it there, it is not easy to find a new protein every time. I have a bioinformatics group here actually. But these guys I have, they basically look into the existing target or known proteins’ structure. They take the protein and try to design new drugs. The bioinformatics guy understands which part of the protein the drug is going to bind on to. In this drug, changes can be made so that it sits better on the target.

Respondent 3 elaborated at length on the nature and use of bioinformatics in the context of the ‘entire spectrum’ of discovery and clinical research.

Let’s first look at the genesis of the term bioinformatics, what it means is, to extract information out of biological dataset and any way you extract information out of this biological data set is bioinformatics. So how do you extract information? The way you extract information is you have large data samples and you do a round of analysis of those data samples, because it’s a question of large data sample, s you need a computer to do it because its not humanly possible to look at so much data. I’ve been working in this area since it is was first known by that name, but anyway, where it can be used it is, it can be used across the board since it is extraction of information from biological datasets, different people call it differently, I mean some people call it clinical informatics, what is clinical informatics, it is looking at clinical information and trying to extract clinical data out of it, so if it is phase one trial or phase two trial and phase 3 trials, you’ve administered some drug to a patient and you are trying to look at the blood chemistry, physiology, the pathology and each of these is a data set and how do you bring all this information together and see what is the effect of your drug, these parameters , to me that is bioinformatics, but people would call it clinical informatics.

So there are no real boundaries and in the discovery phase, genome sequences, protein sequences, DNA sequences, these are very large data sets and even to extract any information out of it, you need to develop your skills and knowledge and
programmes, to get information. And any stage in between also, you may generate a
lot of data sets, as long as it is manually readable and interpretable, then it's okay,
you don't need bioinformatics, if its two or three experiments done on two or three
cell lines, I can manually interpret it, so I may or may not need bioinformatics, but
had it been thousands of experiments on thousands of cell lines, then probably I'll
need a computer to do the analysis and find out what are the relationships among the
different variables. So it can be used right from early discovery phase to mid-
discovery phase to clinical phase basically. But the essence is the same, the analysis
of large data sets to extract information. But classically, bioinformatics pertains to
the early discovery phase."

The respondent’s remarks are interesting not only in the context of his attempts to
demystify technical jargon bandied about commonly by the firms to indicate their
competencies or expertise or the challenges of the research work they undertake but also in
the context of bringing out the flow of technologies, facts and instruments across different
kinds of laboratories in different stages in pharmaceutical research and development.

The respondent however differs from respondent 1 in his comparative assessment of
competencies or the gap between Indian and Western firms in the field of bioinformatics.
The gap is explained more in terms of the unwillingness of firms and government research
organizations to plough money into instrumentation and new technologies and handle failure
in the initial stages and the consequent dissatisfaction and absence of initiative among
scientists to engage in ‘ground breaking’ research.

There was a gap until about 4-5 years ago but I think companies here and institutions
here have put in a lot of effort and the gap is getting pretty much closed...at any rate
I don’t think they have gone ahead, I think there is a socio-economic reason for
it...on this one I’m going to go out on a limb and this is my personal opinion and not
that of the firm. Firms in India and government institutions also do not spend as
much money on cutting edge and forward looking research...therefore there is no
incentive or motivation for a lot of people to do ground breaking research where as
in Europe and U.S., they are willing to take the risk, they are willing to put in the
money, you can take the risk and you can fail also...specifically in the case of CSIR
I want to say, they need to encourage early research more and they should sustain
failures, only then they can surge ahead.
There seem to be some contradictory attitudes expressed here. While on the one hand, there is this obvious pride on the reliance on ‘acumen’ and ‘indigenous expertise’ rather than technology, in the context of the usage of HTP technologies, in the case of bioinformatics, there is an obvious dissatisfaction about the lack of availability of sophisticated instrumentation. This can also be understood in the context of the type of research work carried out by the firm. Since the scientists mostly work on known targets, HTP may not be very useful to them. But, with the narrowing of the patent space and their need to bring down the time taken to produce lead compounds, sophisticated technology and expertise related to bioinformatics would prove to be extremely useful in terms of bringing down lead assessment and clinical evaluation periods.

Failure in ongoing projects is ascribed to incorrect scientific assumptions pertaining to the function of the active locus/ target or the molecule and the lapses in scientific competence of the concerned researcher. As reiterated earlier, the real challenge for the firm is perceived to be, not the generation of candidate drugs, but ensuring that these drugs conformed to the predicted activity, with reference to safety, efficacy and toxicity parameters during clinical development.

Projects don’t succeed for a number of reasons. For instance, you are saying that let’s have this target, which is causing this disease and let’s design this molecule to hit the target. There are two variables here. One is the target and the other is the molecule. If the project does not succeed, what are the reasons? The initiated project is not right and also the molecule designed, obviously you are designing it wrongly or the target is right and the molecule is wrong or target is wrong and molecule is right. This is at the scientific level. So one reason for the failure is at scientific level and the other reason could be the fellow who is doing it is not competent. But in big companies, you can’t live with such incompetence; you understand that this fellow is not right. Incompetence means, this fellow is not doing his experiments right, he has made some wrong assumptions and therefore his results and experiments are wrong, particularly in biology. But those are cases where you can soon find it and sort it out.

Also, you must understand that failure is also different in discovery. Failure, mostly does not take place at discovery stage. Invariably we get a drug. You know, it is not
something which you are just getting as serendipity but you have done some thinking, you have worked together and you got a drug and in animal model it is looking good. Drug invariably fails when it goes into human for reasons like toxicity, side effects, efficacy at the stage of clinical trials in phase-I, phase-II, phase-III. The failure is not there, normally you know, with a good experienced team of chemist and biologists, unless you are talking about a totally new target which has hitherto not been validated. Now sometimes it may happen that people start working on a new target and while validating it, they may commit a mistake. Those are rare cases. Those are stages before a target is even being discovered. When a target has been validated and been discovered, I am generally talking about post that scenario.

In the world of these respondents, side effects are construed as the inevitable ‘penalties’ paid for curing larger medical problems, the more severe for drugs for chronic diseases as they involve prolonged usage. Side effects are also construed as being inevitable in a system of beliefs which perceives drugs as ‘alien’ substances, which, though they possess curative properties, simply by virtue of their ‘alien’ nature are resisted by the animal and human biological system. Respondent 1 stated,

Let me tell you, honestly there is no drug which is safe. Every drug has its own problems but the problem is only minimized to the extent that it does not bother you. See, you must remember one thing that human body, whenever it receives a foreign material – drug is a foreign material – body has its own system of combating anything foreign. Antibodies as you know – body creates these soldiers so called antibodies with in it – to fight something which is alien to it. Antibodies are a kind of chemical that is generated with in the body in response to a foreign invader. So when you take a drug, drug is also foreign, now if you taking drug for one day it doesn’t matter, two days it doesn’t matter. But if you take a drug, over a period of time, for diseases like diabetes, heart failure etc, it’s bound to have side effects. There is nothing called perfection in everybody, every human being, every system trying to acquire perfection. I think drug is also like that.

Today you have a disease for which you are looking for a cure. You don’t have an absolute cure for everything. You are only aspiring to have a medicine which can take care of the problem you are suffering from. You may have to pay a little penalty for it, which may not be a life-threatening or life consuming process. Let’s say you have cancer, cancer is a disease which is definitely results in death if you don’t take care at early stage. Today, the kind of drugs you have in the market, you see, cures the cancer at least in large number of cases, but at the same time you have to pay some penalty for it. Penalty is that you have diarrhoea or lose your hair or all kinds of problems, but what is the option today. But look, if that cancer remains untreated, surely it would result in death. But, if you have a drug which is going to
slow down this process, in many cases it prevents death. At the cost of losing your hair, having diarrhoea, this and that, but that is only for a short period.”

Since no drug is ‘perfect’ and drug safety is perceived as an ongoing process, the business of discovering analogous molecules somehow becomes a medically and scientifically legitimate enterprise as, theoretically at least, they hold the promise of a relatively better cure, not only in terms of curing the disease but also progressively mitigating these ‘penalties’.

Safety of a drug is a never ending process till you see that patients do not have any problems. What happens is that, in-house, we call it pre-clinical evaluation, in pre-clinical stage we try to do those experiments, which satisfies us to a large extent the drug we are using is safe. But, that word safe is relative. Whatever dogs’ study you do, rat or rabbit, I mean its ok. But ultimately, the human beings have to respond to your drug.

This is what we are doing, we are making everyday effort by collective wisdom, talking, discussions, biologists carrying out more experiments, more safety studies. For different diseases, eventually we come up with a drug which is safe, that is, comparatively safe. The safety thing is an ongoing, continuous process and no company or scientist or nobody can claim that has he got the safest molecule on earth. We have not said that we have solved the problem of side effects.”

Side effects are also articulated in terms of different treatment regimens. They are articulated in terms of being more severe and more difficult to predict in the case of chronic diseases in comparison to infectious diseases. These effects are attributed to the accumulation of the residual material related to the drug, which increases due to prolonged usage of the drug. This is cited as the reason for drugs for different diseases having different protocols. These following remarks indicate how drugs are invested with different attributes or qualified differently, depending upon the disease they seek to address. They also point to the porosity between discovery related laboratories and clinical spaces and how the stabilization of laboratory protocols and knowledge regarding drugs occurs through the flow of facts between these different spaces. The qualification of drugs is thus an ongoing
process, where stabilization may occur over a period over a period of time but this is also subject to change.

You have certain medicines you take for chronic treatment, certain you take for acute. What are acute treatments? Say, you fell ill, you have infection, you have been given this drug for two weeks. Obviously you are taking something for a short period. Safety norms for such a drug would be different. Because, you see, what happens is, by taking a drug, it may not cause toxicity. It is only observed in cases where the drug has been given for a longer period of time. In treatment for chronic diseases, you may be taking it for the rest of your life. What happens is the drug has gone into the body and gets distributed. Whatever effect is there, it does for a certain period of time, and you benefit by it and the rest of it goes out of the body but not entirely. Slowly, over a period of time it accumulates in the body. Accumulation of drug in the body, obviously something foreign getting accumulated in the body could have side-effects. You can’t really predict this; you can’t do a trail for the next twenty years.

In some cases, side-effects due to accumulation are nothing, very minor and don’t get detected. In some cases you don’t have adverse effects. In case of acute treatment you are doing treatment only for a short period. So, accumulation is unlikely or very little or even the moment you stop the treatment, after few weeks or few days it will go. So any side-effect arising due to administration of this drug may not as much. So now, you see two different treatment regimes, one is acute the other is chronic. So obviously, the parameters for these two would have to be different. A drug which has been given for rest of your life or for 1 to 3-4 years, are going to be different, have different effects. That’s why there are different protocols for drugs used for these two regimens. That’s why phase-IV is there. Phase-IV development is what - it is research - you try to see what is happening when this drug is given to this community, go to the doctors, go to the hospital, get the data, to know. Dr. Reddy’s have their own centres and doctors who do this, wherever we are selling our drugs, we have it. I am sure other companies also have it. Suppose some centre says that, hey this drug is showing some adverse effect, you will obviously discard the drug, number one and then you work hard, do whatever it is to decrease them. Normally, you know, most of the drugs we or any other company make, these are all generic drugs. I mean, they are already been marketed elsewhere for so many years.”

Notions about quality are articulated both in a normative sense and in purely technical terms. In a normative sense, it is construed in terms of fulfilling the therapeutic promise that the drug embodies, that of cure coupled with minimal side effects. In a purely technical sense, during the discovery stage, if at all deployed, it is associated more with the notion of ‘purity’. However, there is also a caveat here in the sense that the notion of ‘quality’ is felt
to be more relevant to the stage of manufacture of the drug. It is regarded purely as the business of the in-house department and it is separated from notions about safety and efficacy.

Quality of the drug is basically implied in terms of what is it able to address by curing the disease. Efficacy and all or having no side-effects, minimum side-effects that is what would I mean by quality. Quality, when you are making the drug, when you are still in the process of discovering, that quality is basically purity. Maybe the quality term is a misnomer here (in drug discovery), I think. Quality, we normally use internally, when we are making a reason in terms of drug purity. We have a quality department internally. They do not talk about efficacy and safety. They talk about whether it had any purity and foreign material and all that.

The interesting aspect of these articulations is the fragmentation of the notion of quality during the different stages that the drug undergoes. Though the notion of quality in a technical sense might be largely relegated to the notion of purity and delinked from notions about safety and efficacy, during the discovery stage and perhaps even the development stage, the notion of quality implicates all these aspects during the marketing of the drug.97

Though the present section may concern itself with how this notion is deployed during drug discovery and development, it is also largely interested in the process of ‘qualification’ of the drug. The idea of the ‘qualification’ of the drug, implicates not only the notion of ‘purity’ but also other attributes like novelty, safety, potency and efficacy, which are attached to the drug.

Recently, the firm has entered into tie-ups with hospitals like AIIMS, Vellore and NIMS in India, to conduct clinical trials on its molecules, discovered in its Indian R&D centre. Some of these molecules underwent trials in Europe. With respect to the molecules discovered in Atlanta, the firm conducts clinical trials in Europe and Canada. The motivation of the firm to go global with its clinical trials was essentially due to its targeting

97 This will be taken up in Chapters 6 and 7.
the global markets. In terms of the centers chosen for clinical trials, located mainly in Western nations, the firm’s strategies have been different from the strategies of other respondent firms. The company’s recent decision to carry out clinical trials in India may be partially on account of the emerging perception and hype of India as the new clinical hub, the entry of multinational firms for trials, the mushrooming of Clinical Research Organizations and the cost related advantages of carrying out trials locally. The greater likelihood of inducing bias in trial design and management in local settings, especially government institutions and the role of pharmaceutical firms in shaping clinical knowledge of drugs and favorable outcomes were issues on which the respondents typically expressed ignorance or dismissed it as happening in a few cases but largely a creation of media ‘hype’ and ‘negative publicity’. Their discourse was primarily related to the costs and uncertainties surrounding the clinical enterprise, in terms of the use of expensive animal models, the logistic difficulties pertaining to multi-centred trials and studying different target populations and their relatively ethical and cautious conduct in comparison to multinational firms.

The regulatory body is making things very difficult for drug discovery, especially regarding the use of animal models. You know you have to demonstrate safety in animal models, which takes lot of time. They may say more than one species, more than two rodents, dog and monkey and all that. Animal studies are very expensive, especially as you go from rodent to dog to monkey, they say demonstrate safety, demonstrate it for six months. Then when you are doing the clinical trials, they would say, you take a wide range of human population. You should have multi-centred trials. Normally, we go to Europe and Canada. In India, also, we have started doing now. AIIMS, and Vellore and NIMS, we are doing something there. The FDA (US) would not want us to do certain kinds of trials here since you don’t really have a proper system in place here. Reddy’s wants to go to tried and tested centres in Europe and Canada. We have been doing most of our trials abroad in Europe. Only recently, we have started doing something in India. Reddy’s was looking for the global market. And for global market you go by what FDA says. So we are doing it only for our own molecules. Some molecules that we invented here locally, we are doing clinical trials for it here. The advantage that these molecules offer is related to obesity, that in addition to lowering sugar they may also lower cholesterol and so on. Reddy’s is trying to do things in the right way. It’s just that if we don’t do that and if
our data is problematic, then we would end up in litigation. It would be foolhardy on our part to do anything like this at this stage.

What is interesting about this discourse is, while clinical development is admittedly a complex techno-scientific activity, this techno-scientific nature of the enterprise is actually used by firms to highlight their concerns and draw attention from more problematic areas.

Multinational firms are coming here only in certain cases. They may want to test it on a wider range of populations. India still lacks a lot of things, systems, processes, clearance, still there are a lot of problems. Institutional Ethics Committees and all, they do a lot of delays. Expertise is lacking, you don’t have a history of clinical trials in this country. Clinical trials means you need to have good doctors, good hospitals, and data management. Anyway the regulatory body is hardly effective, so you have clinical trial violations; we have to be wary, since it gives us a bad name. In Europe you don’t have all this.

Big companies of course try to get away. Even if they have to shell out some billion dollars as compensation, it doesn’t really matter. But even Merck, due to Vioxx, their image has been impacted. They had to remove their CEO and all that. But they have made their money. Even if they kick out a hundred people, they know how to take care of it. I’m not saying that they don’t care, but they will be more casual compared to Reddy’s in making sure that their data is right. We are looking into things more carefully; we are very particular about our image, since we want to be in the business in the long run.

Lapses in trial data management were articulated in terms of the probability of honest mistakes in assessments of data, the onus on science to be self-regulatory and the political and financial muscle of large multinational companies to influence ‘stringent’ regulatory bodies like the FDA. The rhetorical espousal of the liberal democratic and ethical principles related to self regulation that science embodies may also shift attention from its increasing control over the data presented to the regulatory bodies.

Clinical trials are not done like this you know, nowadays there are companies, contract research organizations, who do it for you. You just have to pay them some money and have a clinical team in your firm to coordinate it and they take care of it for you. They identify centres, doctors, patients, they do data management, churn out the data, they may not really cook the data but they may make mistakes in analyzing the data. You may see some parameters and you may interpret it differently. It’s the interest of the firm also to audit the data carefully, in the case of foreign companies, since it will be going to the FDA and not the local regulatory body. They are very
strict; they follow a lot of procedures. Ultimately you know, its ethics, no scientific study can be monitored in a regimental way by FDA or any other body. Science by its nature should be self-regulatory. If you and I as scientists are going to be dishonest want to be dishonest, what can the regulatory body do? It’s only later on when an adverse reaction happens that you will really know. Now what regulatory bodies do is they go through your material or documents very carefully and they question you at every stage. And then they evaluate. FDA approval is a pretty rigorous process, it’s not easy. But there are companies, big companies, they flex their muscles, they twist their arms and try to get around them. You can’t have a body, which is totally impartial.

In this context, while the firm actively pursues licensing and development arrangements with third parties, it also conducts clinical development of some of the candidate drugs on its own, where it is economically and technically feasible. Its long-term strategy for drug discovery is to engage in clinical testing independently.

The above section examined the ‘qualification’ of drugs in the context of scientists’ everyday routines and practices. The following section, specifically takes up this issue in the context of the firm’s out-licensing of its drugs to a multi-national company, Novo Nordisk in 1997.

The Out-Licensing Episode

During the early days of the firm, in the nineties, the founder had identified diabetes as a potential area of entry for research in discovery research. This was attributed to his suffering from the disease and his identification of the area as potentially lucrative. Respondent 1 elaborates,

In the nineties when Dr Reddy’s set up this discovery centre, there was really nobody who ventured in this particular area. Ranbaxy and others were trying to do it, but not at this level, which we were trying. He had this vision that we must venture into drug discovery and I think, diabetes was chosen mainly because of his interest, firstly, he was a diabetic patient himself and then he was looking at big money, because diabetes, cardiovascular these are life-style management diseases. And this means big revenues and he was obviously looking at the international market and not the Indian market at that point of time. Even today, those pharmaceutical companies who are into these ventures, they, even today don’t consider India as a market, because you know the market is, in US and Europe.
The project involved understanding the role of a protein, PPARS in influencing enzymatic reactions pertaining to the control of diabetes and the discovery of molecules, which helped to produce the reaction. The initial breakthrough made by the firm is largely represented by the respondent as a ‘routine’ kind of science, aided by serendipity.

There was this new target or protein in those days, called PPARS, so he chose that. PPAR is a very common target. It is a transcription factor, it’s a protein. Transcription factors are those proteins that are involved in transcribing the gene. Every human being’s genetic material is coded in genes. This protein helps to encode cells. Cell is the code of life. When cells do not regenerate, then disease sets in, kicking in of factors, malfunctioning at the tissue level takes place. A misreading of this code leads to mutation. That is, this misreading or mis-reproducing of the code leads to the right kind of protein not being produced or the wrong kind of protein being produced. So we tried to look at the effect of PPARS in combating diabetes. So, this target of diabetes was generally considered to be a ‘hot’ target. So we also took this as a target and very early on, we had made a breakthrough and found some candidates. I wouldn’t say there was any great science in it. It was luck, beginners luck, we did it and it happened. There’s a lot of serendipity involved in drug discovery.

The comparator molecule, on the lines of which, the firm commenced its research, was Proglitazone, a drug in the class of insulin sensitizers, which were supposed to help the body utilize the existing reserves of insulin and facilitate absorption of glucose in a better manner in the medical condition of Type II diabetes. The drug had been originally discovered by a Japanese firm, Sankhyo. The firm had subsequently licensed it out to the multinational company, Glaxo Smithkine Beecham for clinical trials. However, the FDA had rejected the molecule on account of its adverse drug effects. The task for the firm was then to produce the advantages of Proglitazone, while at the same time, minimizing its side effects. Respondent 2, who had been involved in the project since its inception mentioned,

In 1994, when we started there was this new molecule in the market called Proglitazone, which was a novel molecule in the diabetic field, the novelty of this molecule was that… the existing drugs, not now but then back in 1993-1994, produced hyperglycemia with respect to Type two diabetes, that is, some problems
of these drugs were, insulin may be there but it cannot act to reduce sugar levels since insulin sensitivity is lost and this drug on the other hand produced euglycemia, that is this class of drugs would facilitate more absorption of the sugar by the tissues, more absorption and transportation of existing glucose to the tissues, functions as insulin sensitizer, it overcomes the resistance to the absorption of insulin. We felt that this is an unmet medical need, and we should look into this class of molecules. And this molecule was novel and it was in different phases of clinical trials. And then my chairman, he got interested and he said, this is a novel way of addressing the hyperglycemic state, and then we started working on insulin sensitizers. We were looking at this molecule, as reference, Proglitazone, which had been licensed by Sankhyo, the Japanese firm to GSK...Our chairman, he used to get the information, this was in the early days ...So this molecule, proglitazone was the starting point for us.

Those were the days before the internet, and we few of us, we had a lot of discussions and debate, you must remember at that time, the world over they were focusing on insulin sensitizers, insulin sensitizers were a novel way of addressing diabetic syndrome especially for Type Two diabetes. So this was an area which we felt we could move around in, there were other areas in which people were already working, end point was a drug which could produce hypoglycemia.”

The project was taken up as much for its potential in terms of generating a new patentable molecule, in an area that had been relatively less explored at that time, as the need felt by the founder to initiate discovery research related efforts. At that time, the firm was in the process of setting up its discovery research centre in Hyderabad, and due to the founder’s keenness on getting the project off the ground, the firm rented space at the National Institute of Nutrition to commence their studies. The institute was also chosen since it had laboratory animals which were diabetic and the tests could be carried out on these animal models. Thus,

Dr Anji Reddy, himself being a chemist, a scientist and entrepreneur, all this amalgamation helped in the visualization of the impact we could have if could have a new molecule come out of our own firm. And moreover, this was a novel and noble way of addressing an unmet medical need. Dr Reddy is what I would call an impatient scientist, though a visionary. At that time, we were just organizing our research lab, there were only walls and a roof, he said, let’s not waste time; we can’t afford a day’s delay. A day’s delay means loss of resources, not only financial but also the sheer pleasure of bringing a needed drug in a timely way into the market. So we leased out a small accommodation in National Institution of Nutrition. At that time, NIN had certain animals which were hyperglycemic and diabetic and they
were all available there. So right from the third month since I joined, we started working there. I’ve been with the firm since its inception and that’s why I can tell you in depth stories about it.

The project also required in-vivo tests on a class of animal, referred to as the DBDB mouse, which was not available in India during the period. The firm subsequently negotiated its way through a series of bureaucratic procedures, involving organizations as diverse as the animal welfare board and the directorate general of foreign trade (DGFT) to import the mice.

So immediately when we were looking through the literature, we found that this particular class of molecules is screened against a type of animal, the DBDB mouse. The DBDB mouse are not available in India, they just mimic the human type two diabetes. This is a very natural way of testing, if you can test. So Dr Reddy’s said let’s import them. Then it was costing about $45 per mouse, which was a princely sum in those days. Then we had never had the opportunity to handle such a small animal in a lengthy session. A host of parameters had to be checked like glucose, triglycerides, insulin levels, and the amount of blood present in a mouse is very less, so OGTT or oral glucose tolerance test which are all similar to the diagnostic tools used by the clinicians. So Dr Reddy’s said we will import these and we worked and nobody had imported these small animals at that time and we went through a series of complicated bureaucratic procedures for the import of these mice. You have to take wildlife, animal welfare board, government of India, DGFT, so many sanctions and procedures, whether the import of these animals would cause any imbalance, so wildlife people’s permission was required. There were of course small delays, but we managed, we were actually the trend setters, I would say because we were the first to import these animals in those days. Now of course every research centre in the country has got these animals. Since we struggled and made a path, it was relatively easy for the other companies later.

A total of about eighteen scientists, six biologists and twelve chemists, were involved in the project. The intense competition involved in coming up with a molecule before its competitors and the founder’s prior expertise also drove the selection of molecules on which tests would be conducted. In a vein, similar to respondent 1, respondent 2 also attributed the success of the project to serendipity and reiterated the role of patentability in driving the ‘leads’ pursued by the firm. The latter factor was also emphasized by dwelling
on episodes where the firm had ‘lost’ molecules due to its failure to be the first to synthesize and patent the molecules among its competitors.

Dr Reddy’s being a chemist, he would involve himself a lot in all this, with the chemistry guys, to make the molecules. We had a small team at that time, there were about six people, and of course I am talking about biology. The chemists were about twelve and the senior management people maybe about four to five and so you can say that there were no delays in communicating across. And you know every day, at four o’clock, at the end of the day, Dr Reddy’s would like to see the results, which were faxed to his office. And then he would go through the results and we would get comments like, oh this interesting and let’s work on this particular scaffold, and he being a passionate leader and scientist, he used to drive us and you know we did not have a lot of bureaucratic procedures. That’s what’s important in drug discovery, time is important and speed and success of course, its all left to luck and efforts are more important than anything else. The results definitely will come and sometimes they will translate into new molecules which will go through all the phases of clinical trials and reach the market. Its sixty per cent luck and forty per cent effort. You have to also have the space to maneuver with respect to Intellectual property because it’s not as if someone else somewhere is not working on it, some other pharma firm. In fact, that’s one of the ways in which we have lost some molecules because by the time we synthesized it and achieved success, we know someone else has already worked on it and patented it. We did patent searches and these cover everything vaguely and they would not give you everything clear cut because it could be used elsewhere. That also means once a broad patent has been covered, you don’t have a way to walk or maneuver on that particular scaffold.

This is because the particular class of molecules or substitutions around the molecule is patented of course. It’s a strategy, to close all the available paths known to you around a molecule so that no body can encroach on your intellectual property. And so we had a glorious take-off and within a year, we could identify very novel molecules.

The respondent also subsequently highlighted how, through a story that appeared in Scrip, about Reddy’s and its research on insulin sensitizers, Novo, the leader in the class of insulin related drugs, during that period, evinced interest in visiting the firm in India, in order to in-license the molecule. The comparator drug, Proglitazone, was supposedly exhibiting adverse effects in terms of hepatic failure and heart related problems. The added advantage of Reddy’s molecule was supposedly that, it had a good toxicity profile in terms of these adverse reactions in comparison to Proglitazone.
Being a small pharmaceutical company then, we were not as big as we are today. So that has helped us and Scrip picked up the story that DRRF is working on some kind of insulin sensitizers, see Novo Nordisk did not have any other molecules other than for insulin, they were scouting around for a small molecule which they could use as a supplement to their main molecule. They were the leaders in anti-diabetic field, insulin preparations, long active, short active and so when they saw the Scrip report, there was some sort of meeting here and they expressed that they would like to visit DRRF. Naturally we will not say no. They came here, saw the infrastructure, and were very impressed.

At that time they were just scouting for some small molecules which could be licensed out to them and they were doing some R&D assessment. We shared some preliminary data on what sort of anti-diabetic molecules we had in our basket and that has impressed them. Then further dialogue happened and we were very fortunate to have a molecule, 2725, they had a wish list, proglitazone was good, it was novel and first in class, and people were having some therapeutic benefit from it, but the problem was that it had some hepatotoxicity and cardiotoxicity. Moreover, after some time FDA asked the company (GSK) to withdraw it because there were some cases of hepatic failure, (in 1999-2000). Our molecule had the lowest safety margin and even though it belongs to the same class, it did not have that much of hepatotoxic liability at all. We didn’t have the infrastructure that we have today to go into short term toxicity and long term toxicity. So we were just beginning, for drug development we need good chemistry, biology, good toxicology support and over and above a good clinical team. So you have several bogies of various expertise attached to the engine, to describe it metaphorically.

The respondent further outlined the gradual process of zeroing in on the candidate drugs from the initially large number of 300 molecules produced by the chemists at the firm, the progressive increase achieved in the therapeutic effects of the candidate molecules and the recourse to delivery systems research and formulations R&D to better their profile.

Synthesis is a very easy task for our chemists who are seasoned and can do anything. Since we knew the scaffold, we were tinkering and fiddling with the class, and around 300 molecules were synthesized at first and you know it’s just a gradual process. Our first molecule had a 30% reduction in sugar and 10% reduction in insulin. We know that some polishing would help us to reach 80%. It’s like a structure-activity relationship. You know which side is blocked and which side is giving a longer duration of action. Small things like better delivery systems, formulations R&D, all these are useful supplements to drug discovery and will help you polish your molecule. So we screened all these 300 molecules and they were all having fantastic activity. But one had to choose the best system. We did not have any automated machines for screening, just simple in-vitro tests followed by proof of concept.
The first molecule to be licensed out was *Balaglitazone*. The second was *Ragaglitazar*, which was perceived as more potent of the two, which therefore was considered more suitable to be taken up for clinical trials.

So they took the first molecule, and the molecule was Balaglitazone, and then the second in the same series was there, Ragaglitazar which was much more potent, so naturally we would prioritize the one which was much better, so Ragaglitazar went ahead.

These molecules were licensed out to the firm for an upfront payment of Rs 3 million, with the understanding that there would be further royalties depending upon the molecules’ performance in being able to live up to their therapeutic potential during the different phases of clinical trials. Once, the molecules reached the market, the arrangement were that the marketing rights of the drug would be jointly shared by the two firms according to their prior agreement. This was also, because Reddy’s as a fledgling firm, did not possess the resources to shoulder the expenses of clinical trials on its own. Respondent 1 stated,

> This is of course due to the maturing of the business and the business strategies. Then, at that time, they (Reddy’s) didn’t have that kind of money. They needed someone to develop their molecule, give them milestone payments, and give them royalties. As you cross every phase of clinical trials, Phase I, II, III, you get some money. Once, it’s approved by FDA, you get some more money. Once, it enters the market, you tell them, you take care of Europe, U.S., I’ll take care of Asia, other markets…Why this happened is also because drug discovery is a very long drawn process.

However, *Ragaglitazar* evidently displayed evidence of bladder cancer in rats in Phase 3 trials. So Nordisk subsequently returned the molecule to Reddy’s. The returning of this molecule was not disputed by Reddy’s since they believed there was some merit in Nordisk’s assessments and Nordisk showed them the relevant data.

It’s a known open fact that not all molecules make it to the market, there are hurdles at every stage, right from the clinical to the manufacturing stage, and there are beautiful drugs for cancer which may not work because of problems related to
commercialization. Now Ragaglitazar went to phase 3, which is beyond than 6 months, because you are dealing with diabetes…so protracted treatment is required, so in the development phase, there is some regulatory requirement regarding carcinogenicity, there was some evidence of bladder cancer in rats which has prompted them (Novo Nordisk) not to pursue it further. You need to understand it’s a good candidate, whether or not it translates into a good drug in human beings, that’s a different story.

However, surprisingly on grounds that the molecule’s efficacy profile was no better than the existing class of molecules in the market, Novo Nordisk also returned the molecule, Balaglitazone, first licensed out to them. Reddy’s, however, believed that the molecule could go ahead and that Nordisk had either underestimated its potential or assessed it wrongly.

Around this time, some employees of Nordisk had quit the firm; they formed the Danish firm, Rheoscience. These ex-employees believed in Balaglitazone’s potential to make it to the stage of commercialization. Subsequently, the two firms, Reddy’s and Rheoscience, entered into an agreement to jointly develop and commercialize the molecule. Respondent 1 had an interesting take on Nordisk’s motives to drop the molecule. The respondents feels that Nordisk’s strategy to reject the molecule was less on account of its therapeutic profile and more on account of strategic and business reasons, the reasons being big pharmaceutical companies’ strategy of buying smaller competitors’ molecules and keeping them on the shelf simply to eliminate competition. The respondent’s argument here is that, merely having a successfully out licensed molecule, which does not go through clinical trials and commercialization, does not confer any great credibility on the discovery related abilities of the smaller licensee firm, and therefore the licensor is successfully able to ward off competition. As respondent 1 put it,

Rheoscience believed that the molecule had some therapeutic potential with all the attributes so we went ahead. But I think Reddy’s also feels that they (Nordisk) dropped it for other political reasons. What happens is that in pharma, big pharma, if they want to kill your molecule, they will take it from you and sit on it. They can
just block your progress; you know there’s a lot of politics. If I am a big company, you are working in my area, I can give you some money, buy your molecule and then just sit on it, I can do anything with it, say its great or its not great, its bad, I can just block your progress. I think the internal politics at Novo Nordisk was also responsible for not taking Balaglitazone forward.

Big companies have no such problems, they have deep pockets, and they can kill a hundred such molecules and still survive. Companies like Reddy’s; they cannot kill a molecule so easily. So the difference is that. So I think Anji Reddy also thought that Novo did not do justice to the molecule (Balaglitazone). Novo said that in animal experiments, they had found some liver toxicity (pertaining to both), so they were not interested. And there was an agreement that if at any point of time, the data showed adverse effects, they could return the molecules. They had all the data with them. And it wasn’t as if they just made such claims, they showed the data.

Once a molecule is rejected it becomes a tainted molecule, no one wants to touch it. But Dr Reddy had the courage of conviction and wisdom and he said that I want to take it (Balaglitazone) forward. Both had different structures, both were rejected on safety considerations. Reddy’s decided to abandon Ragaglitazone and take Balaglitazone forward because they were really convinced that Raga had some problems but with Bala, they were not so convinced. So these Rheosciences guys, those who had worked on Bala at Novo Nordisk, they said it’s a great molecule and we were working with it and we think it has promise, they said they will take it, we will share the costs. So that was reason enough for Reddy’s to continue with it. Also, Rheosciences think that the drug is better; the advantage in terms of body weight gain will not be there. That’s the advantage it will be offering. They are doing it jointly, joint development means, they share the costs and risks, so now it’s gone into Phase III.” This molecule in my opinion would not be such a great molecule. Anyway by the time it comes out, Rosiglitazone (Pfizer’s drug) and other similar molecules would have become more or less generic. The firm is planning to launch Balaglitazone (DRF-2593-307) in another two years.

This view, however, was rejected by respondent 3, who stated the outlicensing company would ensure that there were no conflicts of interest.

They would not sit on the molecule and kill it because the company that takes it out on license has a vested interest in seeing that the molecule gets outside. Moreover, I would hope that the company which has given it to them would make sure that there is no conflict of interest. For these two reasons, the company which is developing the product will not sit on it just like that. If the two companies have done their homework on it, have looked at the ethics and everything. I don’t think the company will sit on it. In that way, you are also hurting yourself by not getting it to the market…Why would it be done if it’s not in anyone’s interest.

Accordingly, in September 2005, the firm entered into an agreement with Rheosciences for the joint development and commercialization of balaglitazone (DRF 2593),
the partial PPAR-gamma agonist, for the treatment of type 2 diabetes. Under the terms of the agreement, Rheoscience agreed to fund all the costs associated with the Phase III clinical trials of DRF 2593 and DRL in return agreed to pay Rheoscience a pre-determined amount towards its share of the development costs. Rheoscience retained exclusive marketing rights in the European Union and China, and the firm retained exclusive marketing rights in the rest of the world.

As per this agreement, Rheoscience also had to obtain all necessary regulatory approvals on the firm’s behalf in the United States. The understanding was also that upon receiving final approval from the U.S. FDA, the firm would have to make a pre-determined milestone payment to Rheoscience. The agreement between the two companies is valid for a period of ten years from the date of commercialization. As respondent 3 stated:

DRL has also retained the right to supply clinical development and commercial quantities of the requisite active pharmaceutical ingredients on arms-length basis to the party that commercializes DRF 2593. After completion of long term carcinogenicity studies, in March 2007, DRF 2593 has entered Phase III clinical trials.

Since then, the molecule has crossed Phase III trials and ostensibly would be launched in the market soon.

The episode is extremely interesting as it highlights how the attributes of the drug, Balaglitazone were qualified differently by different groups including Nordisk on the one hand and Reddy’s and Rheosciences, on the other hand. These variations in qualification were in terms of the technical features like safety related attributes of the molecule. The differences over these technical features were, however, articulated in terms of norms related to professional judgment and the scientificity of their individual evaluations. The
differences over these technical features may also be assessed in terms of their economic interests in relation to the molecule.

The way is which drugs are qualified at the level of the firm is evidently an outcome of the complex interaction of science with market forces. Commercial interests, including the need of firms to get their products on to the market quickly, the existing IPR space, the uncertainties associated with discovery research all combine to exert their logic in medical research conducted in pharmaceutical firms, in terms of pursuing me-too research to mitigate uncertainties involved in the research process, the selection of particular therapeutic areas, the selection of particular molecules as candidate drugs for clinical development in those areas, control of clinical knowledge by firms and the resulting qualification of these drugs with particular attributes.