Chapter 5

GOOD MANUFACTURING PRACTICES AND THE DISCOURSE OF DRUG QUALITY: THE CASE OF LOCOST STANDARD THERAPEUTICS

The present chapter attempts to understand the socio-technical processes shaping the qualification of drugs during the stage of manufacturing and commercial production. In this connection, the chapter undertakes a detailed examination of the every day routines and practices of an organization involved in the manufacture and preparation of pharmaceutical formulations. It also charts the organization’s shift from the local GMP-related drug manufacturing and testing protocols to the ostensibly more sophisticated set of protocols. In this context, it also examines the issues and problems related to the institution’s compliance with these new Schedule M protocols, mandated by Indian regulatory authorities, in the context of their implications for notions about drug quality.

98 The materials for the case study in the present chapter are derived from taped interviews carried out with the managing trustee and the five managerial and supervisory level employees of Locost Standard Therapeutics Ltd., in addition to a focus group discussion with them, during April 2008. Discussions were also carried out with some of the workers in the trust during the detailed tour of its manufacturing unit. Respondent 4, the managing trustee of the institution, a reputed activist and member of the All India Drug Action Network (AIDAN), has carried out extensive research on drug pricing related issues. Respondent 5, the CEO of the trust, has been with the institution since 1987. He holds a B.Pharm degree, in addition to a degree in rural management from IRMA in Gujarat. Respondent 6, a B.Pharm graduate, manages the production related activities of the trust and has been with it since 1999. Prior to joining the trust as Production Manager, he worked with a large firm in Gujarat that dealt primarily in injectibles. Respondent 7, who holds a post-graduate degree in Chemistry (Drugs), is a supervisor in the trust’s quality control department and has been with it since 1994. Respondent 8, who manages the quality control department of the firm, has been an employee of the firm since 1992. Prior to joining the trust, he worked for a leading pharmaceutical firm in Gujarat. Respondent 9, a commerce graduate, manages the financial affairs of the firm. In addition, the trust also utilizes the services of an expert in an honorary capacity for its newly established microbiology laboratory. The employee was not present in the firm during the interviews.

99 As specified in the amendments made in 2001 to the Drugs and Cosmetics Act, 1940. The period for compliance by firms with these protocols was later extended to 2005. The Schedule M amendments invoked a lot of resistance from small firms and subsequent debate among firms, health activists and regulators, which would be taken up in detail in Chapter 7.
The stage of manufacturing and commercial production of drugs is particularly significant in the context of the present study. This is primarily because, though firms qualify drugs in other contexts ranging from research and development to clinical trials to marketing,\textsuperscript{100} the notion of drug quality is typically associated with manufacturing and related testing procedures by pharmaceutical firms. Compliance with the technical features, which this notion of quality embodies, is regarded chiefly as the business of the in-house quality control unit. Thus, notions about drug quality, in this sense, are articulated more explicitly in the stage of manufacturing and commercial production. The present chapter also highlights the implications of these notions about drug quality and the socio-technical processes shaping qualification of drugs for automation and changing skill requirements of work force with respect to manufacturing activities in the sector.

**History of the Institution**

Locost Therapeutics\textsuperscript{101} is a registered non-profitable charitable trust located at Baroda in Gujarat, which was incorporated in 1983. The institution, though registered as a trust under the Bombay-Gujarat Charitable Trust Act of 1956, functions like a typical small scale pharmaceuticals formulation unit.\textsuperscript{102} The trust had its origins in the grass-root level experiences in rural India of a small group of health professionals belonging to the Medico Friend Circle in Pune. It was subsequently set up with the objective of demonstrating that ‘essential’ and ‘quality’ drugs could be available to consumers at affordable prices.

\textsuperscript{100} Reference has already been made to this in Chapter 4, which dealt with scientists’ articulations about drug quality and the processes shaping qualification of drugs in the context of discovery related research activities.

\textsuperscript{101} Also referred to as Low Cost Standard Therapeutics.

\textsuperscript{102} Obtaining a license from Indian regulatory authorities to produce and market medicines commercially necessitates compliance with protocols specified in various schedules of the Drugs and Cosmetics Act of 1940, in particular, Schedule M of the Act. Also, since the sales turnover of the institution is about Rs 3 crore annually, well within the annual turnover specified by the Indian regulatory body for a unit to be labeled as small scale, the institution has to comply with all the protocols prescribed for small pharmaceutical firms.
Respondent 4, the managing trustee of the firm elaborated,

We were doing our share of seminars and workshops and sensitizing. But after some time, we got the feeling; we were not doing anything. Talking and analysis is important but what you need are some solutions. What we were trying to do was to show that good quality medicines can be made at low prices, and I think by and large we have succeeded. We make all generic medicines, nearly all the medicines that appear in the WHO essential drugs list, for primary and secondary health care. There they have got about 354 drugs, here we have about 80-90 drugs. We have almost all the drugs for primary health care.

These articulations about the origin and mandate of the firm are forwarded in juxtaposition to the argument offered typically by large firms that ‘quality’ drugs come at a price.

The philosophy of the trust and the articulations of its employees no doubt vary in comparison to the perceptions largely offered by personnel in a typical firm. What is interesting here is that, though the institution shares notions about the role of instrumentation and protocol adherence in contributing to therapeutically better products with large firms, it emphatically seeks to dissociate notions about drug quality from price related issues. The relation between high prices of drugs and better quality is felt to be justified only in the context of certain high-end formulations. In this context, Respondent 5 elaborated,

There is no rationale when they say, we carry out more tests, bio-equivalence and so on, testing wise we are better, so our drugs are higher priced and they are of better quality. We too carry out all those tests. Maybe in the case of sustained release formulations\(^{103}\), there you need more tests. We don’t do such formulations. So may be there, you can say that. But otherwise, as a general principle, no.

\(^{103}\) Sustained release formulations are drugs where the active ingredient is released into the body at regular intervals. These formulations offer an advantage to consumers in terms of the necessity to consume them only once instead of two or three times in a day.
The trust commenced its operations in 1985. Initially, the institution procured drugs from other firms and then supplied them to its consumers. With the expansion in demand and the customer base, the Trust gradually ventured into manufacturing these products. The trust, however, occasionally doubles up as stockist should the demand arise. Respondent 6, the production manager, outlined the institution’s transition from stockist to own manufacturing thus,

Now we have products which are in very good demand. For instance, just Paracetamol, nearly four five batches go out in a month. That means we sell about six to seven lakh tablets. Our pills for diabetes, we sell in a month, about five lakh tablets. Also, what we do is, if there is a lot of demand for some formulation, we buy it from reputed companies, we stock it and we market it. Gradually, we try to manufacture in our own unit. See in the case of cetrazine formulation, that’s an anti-allergic tablet. First we were only stocking it. We were purchasing it from Alembic. Once the demand rose to above one lakh tablets a month, we started manufacturing it in our facility. We sometimes do that also. We purchase the generic drugs after making sure of quality from wholesalers and then we supply to our customers.

Subsequently, in 1987, it graduated to the manufacture of medicines on loan license. This entailed utilizing the machinery and manpower of other firms to manufacture its products under the direct supervision of its own personnel. The institution’s personnel supplied know-how to these firms and carried out the product and in-process checks. However, loan licensing is felt as problematic since the trust has inadequate control in terms of ensuring that the licensee adheres to all the requisite production related protocols. Respondent 6, the production manager of the firm elaborated,

See it is written here. Manufactured by…and it is marketed by LOCOST. The manufacturer’s name is put in small letters. One reason we are not doing much of loan licensing is also because we are not sure of the quality of their products, basically we have to depend upon the manufacturer’s resources. There are other firms in Ahmedabad, but they are located far away. Here, where we are doing, we go, we tell them this is what we want, we check their facilities. We tell them what our requirements are. We send our people to take the water samples there, we check it, we are not sure, that the procedure is being followed as we know in our unit.
Sometimes, the product is defective, we tell them to discard it or we try to re-process it.

The organization set up its own manufacturing unit in 1993. The initial capital investment required for buying the land, setting up the plant and purchase of machinery was acquired through private funding agencies and donor groups. The factory was shortly set up at Por, an industrial township in the suburbs of Baroda city. Respondent 5, the CEO of the trust, explained,

In 1993, when we started manufacturing, in our own facility, we had 10-15 products. Slowly, our network also increased and we increased the number of formulations. Some of our customers, who were buying one lakh worth formulations, today they are buying five-six lakh worth drugs from us. We have given good quality assurance to our customers.

Locost’s products are not available in the open market. It supplies its products only to organizations engaged in fulfilling the health needs of poor patients. The firm’s managing trustee, a maverick of sorts, who encourages customers to carry out independent checks on LOCOST’s products stated,

In some instances, we have had customers sending our products abroad to test their quality, and these products passed all the tests. Our organization also conducts a social accountability meeting every two or three years, which we encourage our customers to attend.

The organization largely positions itself as a ‘quality-conscious’ body catering to the health needs of the weaker sections of the society. The trust’s products are generic, in keeping with its avowed mandate of not confusing the user with brand names. In eschewing the practices, typically followed by pharmaceutical firms in India, such as employing a large marketing force and selling generics under brand names, the institution seeks to infuse its ‘quality consciousness at low prices’ mandate with credibility. The firm supplies 60 drugs in the form of 80 formulations. Of these, 39 drugs in 52 formulations are manufactured by
LOCOST in its factory. At present, the organization supplies only tablets, capsules and syrups. The syrups are, however, manufactured on loan license. The organization essentially caters to the institutional market. The organization’s customers include mission and charitable hospitals, health centres and dispensaries, non-governmental organizations and a few individuals. Some of its customers include Christian Medical College and Hospital, Vellore in Tamil Nadu, Christian Fellowship Hospital at Oddanchatram in Tamil Nadu, Jan Swasthya Sahyog at Bilaspur in Chattisgarh and Ramakrishna Mission TB Sanatorium at Ranchi in Jharkhand.

The trustee and CEO of the institution are members of the All-India Drug Action Network (AIDAN), an organization that has been lobbying with the Indian government on issues related to rational use of drugs, their affordability, availability, safety and pricing related issues. The organization also engages in health related advocacy. In this regard, it brings out a Gujarathi monthly entitled ‘Apnu Swasthya’, dealing with health issues for the public. It has also brought out the publication ‘A lay person’s guide to medicines’, a guide on the use and political economy of medicine. According to the managing trustee, the prices of the generic drugs supplied by the institution are almost 200 to 400 per cent cheaper than similar formulations marketed by other companies. In addition, the institution produces essential drugs like folic acid, which are not available elsewhere in the market.

The following table provides a comparison between the Maximum Retail Price (MRP) of some of the formulations manufactured by the institution and other popular brands available in the market in various therapeutic categories. The drugs mentioned in the table are generic products. The table provides an eloquent testimony of the pricing vagaries that dominate the Indian pharmaceutical market.
<table>
<thead>
<tr>
<th>No.</th>
<th>Generic Name of drug</th>
<th>Strength</th>
<th>Use</th>
<th>LOCOST MRP</th>
<th>Brand name and manufacturer</th>
<th>MRP (as per MIMS) of these brands</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Albendazole tablets</td>
<td>400mg</td>
<td>Against worm infestation</td>
<td>Rs 1.43 Per tablet</td>
<td>Albezole-Khandelwal Combantrin-Pfizer Nemozole-IPCA Zentel-GSK</td>
<td>Rs 12 per tab. Rs 12.37 per tab Rs 9.75 per tab Rs 16.25 per tab</td>
</tr>
<tr>
<td>2.</td>
<td>Amlodipine tablets</td>
<td>5 mg</td>
<td>Anti-hypertensive (For high BP)</td>
<td>Rs 3.25 per strip of 10 tablets</td>
<td>Amlopres-Cipla Calchek-IPCA Myodura-Wockhardt</td>
<td>Rs 36.86 per strip of 10 tabs. Rs 22.50 per strip of 10 tabs. Rs 15.45 per strip of 10 tabs.</td>
</tr>
<tr>
<td>3.</td>
<td>Amoxycillin Capsules</td>
<td>250 mg</td>
<td>Antibiotic</td>
<td>Rs 11.25 per strip of 10 capsules</td>
<td>Amoxil-Zydus Cadilla Hipen-Zydus Cadilla Mox-Ranbaxy Novamox-Cipla</td>
<td>Rs 31.00 per strip of 10 cap Rs 36.30 per strip of 10 caps Rs 45.00 per strip of 10 caps Rs 43.30 per strip of 10 caps</td>
</tr>
<tr>
<td>4.</td>
<td>Diazepam tablets</td>
<td>5mg</td>
<td>Sedative</td>
<td>Rs 1.30 Per strip of 10 tablets</td>
<td>Calmpose-Ranbaxy Placidox-Lupin Valium-Nicholas Piramal</td>
<td>Rs 22 per strip of 10 tabs. Rs 14 per strip of 10 tabs Rs 19.50 per strip of 10 tabs</td>
</tr>
<tr>
<td>5.</td>
<td>Metformin Tablets</td>
<td>500mg</td>
<td>Anti-diabetic</td>
<td>Rs 3.90 per Strip of 10 tablets</td>
<td>Glyciphage-Franco Indian Walaphage-Wallace</td>
<td>Rs 17.25 per strip of 10 tabs Rs 7.20 per strip of 10 tabs</td>
</tr>
<tr>
<td>6.</td>
<td>Paracetamol Tablets</td>
<td>500mg</td>
<td>Anti-Pyretic (For fever)</td>
<td>Rs 2.90 per Strip of 10 tablets</td>
<td>Calpol (GSK) Malidens-Nicholas Piramal</td>
<td>Rs 10.50 per strip of 10 tabs Rs 9.60 per strip of 10 tabs</td>
</tr>
<tr>
<td>7.</td>
<td>Rifampicin capsules</td>
<td>450mg</td>
<td>Anti-TB</td>
<td>Rs 37 per strip of 10 tablets</td>
<td>R-CIN-Lupin Rimactane-Novartis</td>
<td>Rs 42.39 per strip of 10 caps Rs 57.25 per strip of 10 caps</td>
</tr>
</tbody>
</table>

Source: Compiled by LOCOST. Prices of the other brands were taken from MIMS India Digest, May 2007 (Volume 27, Number 5). LOCOST prices are from April-June’07 price list.

The trust produces drugs in several therapeutic areas. These include anti-bacterials and anti-pyretic formulations, besides formulations for tuberculosis, diabetes, hypertension and cardiovascular related ailments. The institution even tried its hand at producing anti-retrovirals, a few years ago, but the effort did not take off largely due to meager or inconsistent demand for these drugs. The inability to produce high-end formulations in therapeutic areas like oncology and anti-retroviral, is perceived more in terms of raw material costs, the trust’s mandate of keeping low profit margins and the vagaries of the market rather than the absence of adequate skill and expertise or lack of access to sophisticated manufacturing technology. These formulations are also perceived as non-viable financially due to raw material costs and the absence of a dedicated market for the large no of capsules or tablets, amounting to nearly one lakh, produced in a particular batch.
In the absence of demand, the trust has to destroy the entire batch after the expiry date. In this context, Respondent 6 elaborated,

One reason is that the raw material is costly. Any tablet has an API and excipient. Basic principle of manufacturing is the same. You have to go through the same process. So you can make it in the same facility. You don’t need any additional expertise. It’s just that we keep very low profit margins, you know our philosophy. And raw materials for these are really costly. Like in the case of cancer and ARVs (anti-retrovirals). And we may not get consistent orders or market. For e.g. I’ll tell you. We manufactured acyclovir400, it’s an anti-retroviral. People told us, manufacture it, there is lot of demand. We manufactured 40,000 such tablets. And we could not sell it in three years. After 3 years, we had to drain out about 15,000 tablets. We were getting orders, but very small ones. People were asking for 250 tablets, 500 tablets... based on just that, we cannot decide. The same thing happened for some psychotropic drugs that we were making. Some of these formulations now, for ARV and cancer, the process and procedures have come in Indian Pharmacopoeia. We have approval from the state regulatory body for a few ARVs. We can do it; we are waiting because we want to see the demand.

And further,

NGOs keep telling us they require our products. But how much? Minimum batch size, at least 50,000 or one lakh tablets, we have to produce. Then only we can manufacture it. So if it doesn’t sell, it becomes very difficult. It’s not that after expiry, we can re-process it and sell it. Once raw material expiry occurs, then we have to reject the entire batch. We have to destroy it. That’s one thing we are afraid of.

In keeping with its philanthropic mandate, the trust does not employ marketing personnel like a typical firm but supplies its products directly to its consumers. The institution’s principle of keeping Maximum Retail Price (MRP) to a minimum does not permit it to provide margins for wholesalers or retailers. Moreover, its products are targeted towards organizations, which provide health facilities at affordable rates or for charity to poor consumers. Respondent 4 elaborated:

Our marketing chain is different from firms. Our customers are like our marketing agents. They suggest the names of NGOs. We don’t have any personnel from marketing. That is why, we don’t have any stockists. We directly supply to the consumer. So there is no question of keeping margins for wholesalers, retailers and all that. That’s why our MRP is also very less. Now nobody can misuse our
products. Anybody, if they want to sell, MRP is the criteria; excise duty is charged on MRP. For instance, this formulation, we sell it for Rs 3/- for a strip of ten tablets. It’s clearly mentioned, MRP not more than Rs 3.75/-. And that’s inclusive of taxes. So you can’t sell it for more. If they stock it and try to sell it also, they will get only 75 paise more per tablet. Our customers, most of them are charitable institutions or NGOs. Usually, they give these drugs for free. If the patients are capable of paying, they charge them this price.

See our aim is different, essentially to reach out to poor consumers. See for example, TB drugs, if you buy in the open market. It’s going to cost you Rs 150-200 per day. Sometimes poor patients with TB, see they come from the working class, they are masons. Usually they are having TB. They earn maybe Rs 200-250 per day. They can’t spend so much. You have to take a long-term treatment. For a year or two. Even our cost comes to about Rs 45-50 per day. Still, it’s better than what you have to spend in the open market. We are trying to target organizations working for such people.

These articulations also highlight the organization’s struggles to prove its credibility as a manufacturer of ‘quality’ drugs at the lowest prices in a sector beset with ruthless competition over brand power and a marketing logic, which ostensibly equates better quality with costly and branded drugs. The organization therefore sometimes encounters situations where a particular organization or hospital purchases its drugs for poor consumers in its community health programmes and costly drugs made by leading firms or the so-called ‘branded drugs’ for its regular clientele. The respondent’s remarks here also sought to highlight the misconceptions of the average consumer on generics. The notion of ‘branded generics’ was also felt to be a misnomer, a creation of the market, since generic drugs in a particular category usually possessed the same active ingredient. Respondent 6 exclaimed:

Even in these organizations, like this Christian missionary hospital in Tamil Nadu, I was telling you about, they source medicines from different places. For community health programmes, they are taking formulations from us. But in the case of other patients who come to the hospital, they are sourcing local medicines. They want branded generics or medicines. There’s no such thing as branded generics. It’s inaccurate. All generic drugs in a particular category will usually have the same active ingredient. But they are sold under different names, which is something we
see only in India and nowhere else. So, where’s the question of brands? Again, some people have this very wrong impression, bad impression about LOCOST. They think oh, LOCOST means low quality. We are working to prove that wrong. So many times, it has happened, we have had to fight, to show, to prove, that our quality is good. One thing is because of our name, LOCOST, and also because we are selling at the lowest price. So they think maybe quality is not good. That’s the normal impression people have.

It is for the reasons mentioned above that the Trust prefers to go by the name of ‘Locost Therapeutics’ than the original ‘Low-Cost Standard Therapeutics’. The respondent also provides the example of a leading firm to reinforce his earlier point.

I’ll give you an example. I showed you this product dissolution apparatus that became mandatory as per our Indian FDA two years ago. Do you know, when Smithkline Beecham first tried to initiate Crocin in the market, it failed this test. It had come in the papers. What is Crocin? It’s just a paracetamol tablet. But brands sell and people think generics are bad. But it’s the same drug.

**Good Manufacturing Practices and Revised Schedule M Protocols**

Before undertaking a detailed outlining of the every day practices and routines of the firm, it would be useful to briefly elaborate on Good Manufacturing Practices and Schedule M protocols. Good Manufacturing Practices (GMP) constitutes an international set of guidelines for the manufacture of drugs and medical devices. These guidelines may vary from country to country, depending upon specific regulatory requirements. In recent years, GMP protocols are being adopted and followed in over 100 countries, either in the form of regulations (Japan, Korea and the United States) or Directives (European Union), Guides (United Kingdom, India) or Codes (Australia). In India, the production, import, distribution and sale of pharmaceuticals is regulated by the Drugs and Cosmetics Act of 1940. Schedule M of the Act classifies the various statutory requirements mandatory for all drugs, pharmaceuticals and medical devices as per good manufacturing practices (GMP). Schedule
M was first revised in 1986, when the concept of GMP was first introduced in India. The Central government subsequently revised the Schedule M protocols in 2001 to harmonize it along the lines of World Health Organization protocols. These protocols included specifications on infrastructure and premises, environmental safety and health measures, production and operation controls, quality control and assurance, stability and validation studies. The implementation of these protocols being difficult in a fragmented sector, several extensions were allowed by the government before it was made mandatory in the year 2005.104

The revamped Schedule M protocols involved several amendments, which were deemed mandatory for firms and other institutions involved in the production of drugs and medical devices. In this context, respondent 5 elaborated,

A lot of things were made mandatory, things like, you have to maintain a ratio of 1:2 between constructed areas and surrounding premises, you need a validated water system, disposal system for waste, environmental control, and also you have to ensure constant supply of filtered air through Air Handling Units. Earlier, we used air conditioners, now they said; in this new Schedule M, you need to have AHUs in all production areas so that environmental pollution won’t be there. Then you have designated areas for production, quality control, storage etc. Then you had to have dedicated production facilities for some potent drugs, the idea being, you have to prevent cross contamination. Then you have constant in-process and operational checks, stability studies of the drugs in different storage conditions, detailed documentation. I’m telling you the main ones; there are a whole lot of these things.

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104 See revised Schedule M guidelines as mentioned by Central Drugs Standards Control Organization, Ministry of Health and Family Welfare. Accessed from the website www.cdsco.org.in. Website accessed in May 2008. The contestations pertaining to these revised guidelines have been examined in detail in Chapter 7.
The amendments thus included detailed specifications pertaining to the ratio between the constructed areas and surrounding premises, validated systems for water and waste control, environmental control, in-process checks and detailed documentation.

**Manufacturing and Quality Control in the Institution**

The present section provides a brief account of the layout of the production unit and the every day routines and practices in the institution in relation to its manufacturing and quality control activities.

The institution has dedicated production units for manufacturing products declared to be potent drugs under the Schedule M provisions. *Betalactin* products like *ampicillin*, *amoxicillin* etc. are manufactured in a dedicated unit. The trust had to shift its laboratory for the creation of the *Betalactin* facility. There is a dedicated space for the storage of raw materials, both active pharmaceutical ingredients and excipients, as per revised Schedule M requirements. Except for *Betalactin* related products, which are stored in the dedicated facility, raw materials for all the other products are stored in this area. An automatic weighing scale is used to weigh these raw materials. The walls of the production unit have curved corners to prevent the accumulation of dust. This is specified as mandatory as per the new Schedule M norms. The institution does not manufacture syrups since that would again require a dedicated unit and an additional outlay of Rs 20-30 lakhs, which it cannot afford for the present.

The drums containing the raw materials, both active pharmaceutical ingredients and excipients, are dusted with a blower and subsequently brought into the raw materials unit. Here, the two quality control personnel check and approve the samples. Once the raw materials are approved, the excipients are weighed and subsequently mixed with the active ingredients. Usually, excipients or inert materials like calcium phosphate, starch etc are
added to the active ingredients in the proportion of 150 grams: 4 grams. These materials are then taken to the manufacturing area.

The trust sources the API from large companies like Lupin and Ranbaxy. The raw material costs amount to nearly 70% of the firm’s manufacturing costs. The margin of profits from its products is very low compared to an average firm since it sells to charitable institutions. These charitable institutions also benefit from the transaction since they usually distribute the drugs for free or at maximum retail prices (MRP) to the patients.

The storage facility is air-locked, with reverse laminar flow provided by the recently installed air handling unit, to prevent contamination from other production facilities. The air handling unit, mandatory as per the new Schedule M requirements, apparently ensures that there is no contamination of the materials inside the facility with other areas in the production unit. The equipment, which costed one lakh rupees, was sourced locally from Ahmadabad. Adjacent to the storage area is the quarantine area, where finished products, tablets and capsules, are stored. Once the testing of the tablets and capsules is completed and has the approval of the quality control unit, the drugs are shifted to the bulk packaging and blister packaging section.

Formulation and packaging is typically done in accordance with ‘good manufacturing practices’, specified under Indian drug regulatory protocols. The products are produced in batches through a campaign regimen. At the end of a typical production campaign, the equipment is cleaned and another product may be formulated and packaged, utilizing the same equipment and personnel. The major purpose of these activities is to convert the raw materials into a finished and usable form. The common dosage forms of pharmaceutical products include
tablets, capsules, ointments, creams etc. The institution largely engages in the manufacture of
tablets and capsules. Syrups are generally outsourced and then marketed by the institution.

The production of capsules and tablets is a linear process involving processes like
mixing and granulation followed by tableting or encapsulation. In the institution, the tableting
room has a mixer, in which powder mixing is carried out. Here both tablets and capsules are
manufactured. Capsules are manufactured in strengths of 250mg and 500mg. Batch size
decisions are based on the capacity of the mixer. The charging of materials here, the active
ingredients and the excipients, is done manually in the mixer. In large firms, however, the
charging of materials has been automated, ostensibly to avoid contamination by human hand.
The number of tablets made depends upon the strength. If the tablets are of 4 milligram
strength each, up to six lakh tablets can be produced. If they are of 500mg strength each,
around one lakh tablets can be produced. Subsequently, a paste of starch and gelatin, which
has a dough-like consistency, is made and added to this mixture. It is passed through the mill
and subsequently dried in a fluid bed dryer. This process is referred to as milling. Earlier, the
firm used a tray dryer. Respondent 6 elaborates

The advantage of the fluid bed dryer is in terms of uniform drying. It is faster and
regarded as more hygienic. With a tray dryer, it is done manually. If you disturb it,
once the process is over, you have to reposition it and fix it. This leads to lot of
wastage of materials. The fluid bed dryer is quicker; one batch can be made and
tableted per day.

Once the mixture is dry, it is passed through a sifter, which separates the dry
granules and white powder. Then these granules are again taken to the mixer. The granules
are lubricated with excipients since they do not have free flowing capacity during the mixing
process. Once this is done, the powder is now ready for tableting.
It is worth noting that detailed instructions related to specific manufacturing activities are pasted near the concerned machines in the production facility. These are known as Standard Operating Procedures (SOPs). The SOPs for quality control are prepared in English and put up near the concerned instruments in the quality control unit. However, the SOPs for the production facility are prepared in the local language. Within the trust, these SOPs are prepared by the production manager and subsequently translated in the local language either by one of the employees or given out for translating. It is worth noting that these SOPs generally involve fragmentation of the production process into specific operations, which are then sought to be described as precisely and minutely as possible. These are then explained in detail to the workers. This is because, in general, queries on adherence to manufacturing processes and standards are generally directed to the workers by drug inspectors. Respondent 6 explains,

These SOPs are given to the workers, explained and they are made to understand in detail. Because the drug inspector asks them the questions. The basic principle is, what you do, you write.

In the tableting unit, there are two machines, about a decade old, in which the powdered mixture is compressed into tablets without modifying the physical nature of the material. Parameters like weight, pressure and hardness are set and periodic, usually hourly, in-process and laboratory checks are carried out during this stage and entered into the batch production records. These are carried out in order to ensure that the product meets the purity, safety and other characteristics that it purports or is represented to possess according to the Indian GMP standards. A variation of 5% is allowed for from the requisite standards. Also, another basic principle here is ‘not documented, not done’. Respondent 6 added,
We have two machines, 16 stations and 27 stations. That is, in the 27 station, 27 perches are there, with two hoppers. Here smaller tablets up to two and half to three lakhs are made per day through compression. Bigger tablets, you may get around one and a half lakh. The machinery here was purchased about 10 years back. Here, weight, pressure, and hardness can be set. In-process testing is done, in laboratory and here also. Every one hour the checks are done in process. About 20 tablets may be taken out for checking at a time. There can be variation of only around 5%. Then you should enter it in the batch production record. Dissolution test is also carried out.

The unit has a tablet disintegration test apparatus for the in-process checks. The final product disintegration test is carried out in the quality control laboratory but the two quality control personnel also check it periodically in the capsuling unit. The unit also has a pliability tester in order to ensure that the tablet withstands its shape and size till it reaches the end user.

A crucial difference between US-FDA approved machines and those used by LOCOST and indeed in general by most of the small and medium scale firms, which produce tablets for the Indian market, is that the US-FDA machines are glass enclosed, all the processes are automated and the in process checks are carried out through computers attached to the production unit, where as in the case of LOCOST, the checks are carried out manually. The automation of these processes and tests ostensibly prevents contamination and human error and ensures detailed documentation. The utility of such automation, given its impact on the small scale sector, is contested by the respondent who views them as corporate strategies for ‘weeding out’ smaller players from the market.

U.S.-FDA machine will be totally enclosed and not open as in LOCOST. Also more documentation is required there. It will be totally glass enclosed. Their idea is that this will avoid contamination and human error. But it’s not very necessary. In today’s world, small players are being weeded out. SSIs cannot survive. We are seeing that happen. Anyhow, we have a clear market. We know to whom we are selling.
In addition, there is also a tablet coating machine in the section, where the tablets are coated with a sweetened or aqueous solution to mask their bitterness, offer protection from moisture or impart distinctive colours to the tablets to facilitate patient recognition.

In the dedicated Betalactin facility, there is an automatic capsule loader, where around 300 capsules are accommodated in one batch. The empty capsules are loaded automatically, and then the upper half of the capsule is removed with the upper plate of the loader. The powder is subsequently weighed and per plate for amoxicillin capsules of 250mg strength, about 80 grams are weighed and filled manually. The powder is placed at a particular point in the loader and the machine is started so that the powder spreads and the lower halves of the capsule get filled with the powder. The top halves of the capsule are then fixed to the filled parts and pressed by the loader so that the capsules get locked. Subsequently, about 20 capsules are removed from the loader for the in-process checks. Again, the weight has to fall within a pre-determined range as per pharmacopoeial norms. Usually about one gram extra or eighty one grams are filled in the plate of the capsule loader in order to compensate for any losses during the process.

The institution possesses semi-automatic capsule loaders in its general encapsulating unit. In semi-automatic mode, three workers are required at a time to carry out the encapsulating process. In automatic mode, only two workers would be required, one to operate the machine for filling in the powder and another to check the capsules. The capacity of the automatic loader is about one lakh capsules per hour. That much capacity is not required by the Trust at present since its present monthly requirement as per market demand is only about one lakh capsules. Consequently, the Trust has sought permission from the state drug authorities to use the semi-automatic loaders in its general capsule facility by demonstrating
that it is able to meet all the required quality-related protocols through these machines. However, for the Betalactin facility, as mentioned earlier, the Trust has purchased an automatic capsule loader, in accordance with the new Schedule M requirements. The capacity utilization of this loader is only around 30%. The example provided by the respondent attempts to invalidate the argument about the correlation between automation and better quality, sometimes provided by regulators and large firms.

Since the automatic machine would cost another Rs 4-5 lakhs, we manage with the semi-automatic machines in the general facility and have sought permission for this. Also that much market demand for our products is not there at present to justify the investment. The drug inspectors, sometimes they say yes and sometimes they say no. But quality wise, we are getting 100% here, so there is no problem about that. It’s not like you always need automation to fulfill quality requirement. But in Betalactin unit, we are having automatic capsule loader as per Schedule M requirements. They (the drug inspectors) say it’s necessary to avoid contamination and all that.

There is a separate capsule section, which is a multi-purpose facility, where different kinds of capsules are produced such as rifampicin, doxycycline, etc. This facility is utilized more compared to the betalactin facility. Here, again, the capsules are produced in batches. On finishing a batch of a particular drug, the machines are washed thoroughly, tested, checked for particles and impurities before commencing production operations for the next batch of another drug.

The Betalactum facility also has a separate packaging unit where capsules are blister-packed and strip packed. But the institution feels it is a dead investment since capacity utilization is not there. On an average, the facility is utilized only for a week’s time in a month. The rest of the time the firm engages in other production activities such as manufacturing drugs like paracetamol, rifampicin, doxycyclin etc and a host of other drugs in the multi-purpose capsule and tablet facility, which has its own blister and strip packing section. Two workers are required for the packing related activities at a time with the semi-
automatic machines possessed by the trust. In the case of automated or online packaging, the worker requirement would increase to four personnel at a time. Respondent 6 described the process of strip packing thus:

A PVC roll gets heated and subsequently cooled; it comes over the pocket and takes the shape of the individual capsule. The capsule is fed through a hopper, it gets filled in the strip and the PVC gets fixed over it. It then gets cut into 10 strips. Here two workers are required, one for doing the filling and one for the checking. If online packing were to be done, two more people would be required. So with automation here, actually more people would be required. There is also a blister packaging machine, with the same function. Certain capsules have to be packed in strip pack, since in blister pack sometimes moisture will be there. Strip packing is absolutely moisture free. Both these types of packing are aluminium-based. Certain drugs like ranitidine (aspirin) or ethambutol (a TB drug) absorbs moisture, so you have to do strip packing. Then there is a capsule quarantine for general capsules, this is again a Schedule M requirement. Since we don’t have anything there right now, we keep other things. When the capsules come, we will have to store it there. This quarantine room has to be air conditioned at all times. These are all as per revised Schedule M specifications. These strip packets have to packed in polythene covers, since even if the slightest moisture gets in, it becomes watery.

The respondent also outlined the issues related to capacity utilization of the plant. The perception of the Trust is that the added financial burden posed by the new Schedule M related investments in machinery and infrastructure does not really translate into greater capacity utilization of the production facility in the absence of consistent demand for its products, especially Betalactum-related products.

I would say with tablets, we are using almost eighty per cent in terms of capacity utilization. But not in the case of capsules. In capsules, our capacity utilization is only about 30%. Especially in Betalactum related products. But we are producing some general capsules also now. We are not producing syrups. Because of the extra investment required. Now in Schedule M, like for Betalactum, you have to make a separate unit there also.

The Trust also possesses a storage godown, where the tablet and capsule strips are packed according to the orders placed by its customers. The godown possesses jars, pouches and bulk packs of different shapes and sizes. The Trust is particular about printing all the
necessary indications and contraindications on the strips in accordance with regulatory requirements, including details such as name of the generic drug, its batch number, expiry date, MRP and the Schedule that the particular drug belongs to. It does not usually stock material in excess of the demand, except in the case of syrups. Respondent 6 explained.

So, in this godown, our workers pack according to the order. Here we have different kinds of jars and bulk packs. This is a 1000 pack. There are pouches of different sizes, 2*500 packs, and 10*100, even we sometimes give 5*100 packs in one jar. You can see here. All the indications and contra-indications are printed on the blister strips and regular strip packets as per regulatory requirements, with details of name, batch number, expiry date, MRP, even which Schedule the drug belongs to, say Schedule H. Based on the order we receive from our customers, we plan it. We don’t stock any medicines. Only syrups, which we outsource, based on demand. Otherwise, depending upon demand and order, we produce.

On the conclusion of the tour of the production facility, the researcher is also conducted on a tour of the chemicals testing room, quality control laboratory and microbiology laboratory on the premises of the plant by the two white-coated quality control personnel. These rooms, like those in the production unit, have a highly sterilized ambience, with a variety of instruments placed on gleaming slabs running through the length and breadth of the room. The centre of the room is empty and white-tiled, presumably to facilitate free movement of the materials. In the chemicals testing room, there are instruments used for the testing of the raw materials and finished product. In-process checks are also carried out. All these checks are carried out as per Indian pharmacopoeia and the new Schedule M requirements. Respondent 7 elaborated on the various instruments and techniques used in the room.

This is our chemicals testing room. Here we do the testing of both the raw materials as well as the finished product, using the titrametric method. We use the oven and furnace here, to determine the water content. That shows us the percentage of moisture in our raw material as well as finished product. We also have to determine the percentage of ash in the raw material. So what we do is to put one gram of the
sample in the furnace for one hour at 800 degrees temperature and moisture presence should not be more than 0.1% as per the Indian pharmacopoeia. SOPs are not required for the oven and the furnace.

Respondent 8 provided a detailed explanation about the flow of materials and finished products between the production facility and the instrumentation room, again stressing on its adequacy as per Indian pharmacopoeia and Schedule M requirements.

Whatever equipment we are using currently here for this purpose, it is sufficient for Schedule M. In our instrumentation room, we have to use air conditioners and maintain 27 degrees temperature,\textsuperscript{105} since there are costly and sophisticated instruments. By using instrumentation like the spectrophotometer, we are using the instrumentation to determine the percentage of purity of the raw material and the finished product. The incoming raw material is sampled and then tested as per Indian pharmacopoeia. After that, these raw materials proceed to the production unit for manufacturing and then it comes back for testing of the finished product. This is also as per Indian pharmacopoeia requirements.

The respondent also elaborated on the tests carried out by the two personnel in accordance with GMP requirements, stressing on their individual efforts to better Indian pharmacopoeia standards in the Trust terms of capsule and tablet absorptivity levels. The example provided by the respondent offer an interesting insight into the potential for firm-level variability in quality control standards and the Trust’s efforts to augment product quality in terms of purity or absorptivity of the tablet or capsule in the body with a similar set of instruments and at no increased infrastructure or instrumentation costs.

\textsuperscript{105} Since the unit is located in Baroda, Gujarat, day time temperatures can be quite high, rising up to 44°C during the summer months.
maintain this limit. Generally our products get 95% of absorptivity in our body. But the lower limit specified by Indian pharmacopoeia is only 80%. In these small ways, we try to ensure better quality of our tablets and capsules.

Respondent 8 also provided a detailed account of the various quality control procedures carried out in the instrumentation room. The Trust uses locally sourced as well as imported instruments for this purpose.

See here, a different instrument is used for testing the dissolution rate of the tablet. Different products have different limits and different time of absorption and dissolution. We use the raw material of the tablet as well as weight for the testing purpose. Earlier we were using the manual balance, but recently we have purchased the electronic balance for this purpose. All these instruments were required in the earlier GMP also before new Schedule M. This is a titrator, another instrument to find out the percentage of water in our raw material. As well as in the granules, which we have prepared through compression. This is the test apparatus, which we use because when the raw materials are packaged and they are transported to customers, there may be some breakage, so we use this apparatus to control this. We have to maintain the percentage, not more than one percent. We use a moisture garage, to find out the percentage of water in our granules. This is seen in the scale in the instrument. We put the powder, approximately 5 grams and subject it to heat. After 5 minutes, you get the percentage of water on the scale. Then there is the ph meter, to determine the acidity and alkalinity in our materials. We have a spectrophotometer purchased in 1992. Recently we purchased a new one. As the machine grows old, the accuracy reduces, so we have to purchase new ones. This is IN or the infra-red spectrophotometer. This is Japanese equipment, the brand is Shimatzu. It is used only on some days. It depends upon the particular product or sample. We have imported it from Japan.

The Trust claims to have incurred an expenditure of approximately 25 lakhs on its new quality control equipment, including the recently set up microbiological laboratory. Respondent 7, while elaborating on the functions of each of the instruments, stresses on the philanthropic mandate of the Trust. His articulations repeatedly emphasize on the commitment of the Trust towards fulfilling and bettering the standards of its products since the early nineties and not merely towards compliance with the new Schedule M requirements.
This is the spectrophotometer we use to find out the percentage of purity of our products. It is attached to a computer since we have to generate reports. These reports are basically in-process reports, relating to procedures used. In between also, we carry out the process checks. A typical in-process report would have these things. This report is the tablet format. In the tablet format we are doing the average weight and weight variation of the tablet during the process. We go to the production unit and take the samples from the machines and then we test these things, the average weight of the tablet and the weight variation. Some tablets may exhibit plus or minus seven percent, some plus or minus 10% and within this plus or minus 5% rate, we check the variation. And then we have to check the pliability of the tablet, so that it doesn’t break during transportation, then hardness test, then again dissolution test. This is the in-process test done during compression. There is a similar format for capsules also. We also have to carry out calibration tests, in order to find out whether our instruments are okay or not. At present we have two employees in our quality control lab to carry out these tests. That is myself and our quality control manager. We do both quality control as well as quality assurance. Most of the instruments in the firm have been purchased in 1992-93. Only the spectrophotometer is purchased recently. Spectrophotometer is useful in determining the percentage purity of the product and the percentage purity of the raw material. We have majority of these instruments at the outset itself. None of these instruments we have purchased specifically for the purpose of satisfying Schedule M. So we all are quality conscious from before. Our Trust is not for making money but to give better quality products.

The respondent also elaborated on some of the new requirements for Schedule M like stability tests. These tests, conducted over a period of time, provide an insight into how quality related parameters are viewed as not related merely to real-time tests carried out during and immediately after production activities but also impinge upon the potency, purity and shelf life of the product during its marketing and distribution stages.

The stability tests are a new requirement for Schedule M. This is our stability oven and we are using this to maintain the stability of our products. We take samples of our tablets and capsules and use this instrument to test real-time stability and also stability over a period of time that is one month, two months, four months and six months. This is a new requirement as per Schedule M. This instrument assures us that our products are stable. That is we are controlling the purity of the product. Some products, over a period of time, the percentage of purity gets degraded. If we find that this is happening, then we do some addition in the product or change some material. We try to control this during our production. The instrument for this we have purchased from Bombay.
The microbiological laboratory is, however, a new acquisition, mandatory as per the new Schedule M protocols. The laboratory contains an autoclave, for sterilization and microbiological testing. Here, the personnel test the water for certain requisite levels of purity, in addition to product samples. In big firms, however, such autoclaves may be considerably larger in size. The advantage is in terms of being able to test a larger number of samples at a time. The laboratory also contains an incubator through which certain specific temperatures are maintained. The room is generally air-locked to maintain a sterile atmosphere. This practically involves the use of a laminar flow to filter the air, whereby it passes through one end and comes out filtered at the other end. Also, when the door is opened, in case of contamination, the instrument sucks the air through one end point and the air is filtered and released through another end point. This instrument, again sourced locally from Bombay, is deemed as mandatory as per Schedule M provisions. The laboratory was installed by the Trust in early 2007.

In general, different countries formulate their own pharmacopoeia depending upon what testing requirements are regarded as mandatory to conform to certain predetermined standards. The two quality control personnel in the Trust, however, did not have any familiarity with the tests required for compliance with US-FDA protocols.

**Schedule M, Automation and Drug Quality: Issues and Problems**

Subsequently, a focus group discussion with the founder and managing director of the trust (Respondent 4), the CEO (Respondent 5), the Production Manager (Respondent 6) and the Accounts Manager (Respondent 9) highlighted the issues, problems and absurdities
associated with the implementation of the new Schedule M protocols by the local regulatory authorities and its compliance within the Trust.

In the context of the differences between the earlier GMP and the current Schedule M, these were perceived in actual terms as being not so much in terms of space or infrastructure requirements but more in terms of equipment requirement like air handling systems, water systems and microbiology related instrumentation. The articulations of the Respondent 6 sought to highlight how compliance with the new requirements had not led to any huge difference in terms of actual quality of the drugs as such, but was useful primarily in terms of streamlining of all quality checks and ensuring that all the necessary protocols were carried out within the plant premises itself instead of being outsourced.

As far as we are concerned, we are producing the same quality drugs, quality-wise there is not much difference, but looking at the cleanliness aspect, it is helpful. Earlier, having a microbiology lab was not considered necessary, it wasn’t there in the previous GMP, it was optional, one could get one’s products tested from outside but now it is mandatory. Facilities for testing should be part of the firm itself. That is the objective of the regulators. With the microbiological equipment, we do testing, if there are any pathogens or impurities in the drug, we do assays, what are the efficacy levels, percentage of purity and so on. Earlier, we were outsourcing it to some testing or QC labs.

Respondent 5 expressed reservations from a cost-benefit perspective, wondering whether the steep costs were justified given, what they dismissed as, marginal improvements in process or product quality.

Anything you add to a system, it will obviously make a difference. Now it’s just a question of cost-benefit. If you have a microbiological lab of your own, or an air-handling unit or a new water system, there is going to be a benefit, no two opinions about whether its going to improve your processes, but the question is about the increased costs, for us to upgrade it took about 75 lakhs. Now for this marginal or incremental improvement in quality, whether it’s worth the 75 lakhs that you’ve put in, that’s the big question.
These reservations were echoed by Respondent 4, along with anxieties related to whether the steep costs involved in the upgradation would translate in terms of better sales prospects for firms or be eventually passed on to the consumers in terms of highly priced drugs.

Our whole factory costed us 50 lakhs, of course that was 15 years ago, but this upgradation has costed us 75 lakhs. If I or any entrepreneur pays up and installs all this, finally he’s going to pass it on to the customer, so whether this marginal improvement is quality is really needed. Sometimes, upgradation is there, but where is the market? Owners are thinking, even if I am upgrading, where I am getting my money’s worth, in terms of more sales, things like that.

These articulations, however, do not seek to question the necessity for these quality-related checks by the regulators since they dovetail with the Trust’s avowed mandate. There is also the perception that as far as the nitty gritty or intricacies of these checks are concerned, the new Schedule M protocols do not really differ much from the old GMP in terms of emphasis on the process rather than mere inspection of the final product. Thus as Respondent 6 states,

In terms of in-process checks, as far as we are concerned we were doing it earlier and we are doing it now. In terms of what these checks are, there is no much difference between the earlier GMP and the revised GMP. In manufacturing, in terms of all the different stages, what you try to do in these in-process checks is to ensure that what you are doing, you’re doing it fine, since the cost of reprocessing it later would be much higher. That’s the rationale of in-process checks. So quality is not an end point but it’s a process which you follow throughout all these stages. This philosophy was not there earlier, but it has been there since the eighties, at least after I passed out, this philosophy has been there that the quality is not just part of the final product but the whole process has to be maintained.

The respondents, however, criticized the need for extensive documentation of specific work tasks related to the production process. Their articulations stressed on how they were efficient with the implementation part of the quality protocols and how on their
own, they had initiated stringent checks on parameters not mentioned in the Schedule M protocols due to their organization’s commitment to better the quality of their products. At the same time, they also admitted their inability to comply with the detailed documentation related protocols at specified intervals due to the inadequacy of their work force. Their diatribes against the logic of linking detailed documentation with assessments about the quality of their products or manufacturing processes also questioned the inefficiency of the system in exposing malpractices.

Respondent 6 opined,

Schedule M hasn’t led to any decrease but an increase in the workforce, since it requires so much of documentation. All very unnecessary we think.

Respondent 5, in a similar vein, added,

Most of their (regulators’) assessments of quality are based on your documentation. Documentation can always be cooked up. You do it, you don’t do it, but if your documents are ready and okay, then they are fine with it. You know the philosophy, not documented not done. One problem is, we are very good with the implementation part of it, since we’ve been quality conscious from the start, there are a lot of things we do that we haven’t been asked to do, but we are not very good with the documentation part of it. One thing is after the microbiology lab has come up, there are certain things that we do regularly, we test the water quality regularly, we take samples from the wall and we check whether there’s contamination. These are not things which are mentioned anywhere. These are things you do because you believe you have to do it. The problem is some times because we have a work load or less work force, we wouldn’t be doing it regularly, say after every seven days, we would be doing it after ten days, four days, twelve days, depending upon our load various other factors but that would not be acceptable to them because if you set up a procedure and say you have to do it every seventh day, then we have to comply with that. So to that extent we may not be compliant, but we feel, the whole process itself is not required.

Their skepticism about the efficacy of Schedule M inspections in bettering drug quality also stemmed from their perceptions that the methods used by drug inspectors to assess compliance were piece-meal and hasty. In this context, for the most part, one finds that there is no questioning of the Schedule M protocols in principle. Rather, it is the
inadequacies related to their implementation that is the source of discontent. As Respondent 5 put it,

See, what happens in Schedule M is, the inspector comes for one day in a year, maximum two days or say three days, he asks, are your documents there, are your samples there, have you done all the tests, but the actual philosophy behind Schedule M is, you have to do these tests, documentation regularly and if there are any defects in your process or products, you have to change it, but then the person who comes, when they do their field survey, it’s a somewhat dim approach, since his attitude is, is everything there physically... then okay...as long as things are there on paper, it’s fine.

The remarks made by Respondent 4 also highlighted the burden of recurring costs in preventing scrupulous implementation of the protocols by firms.

There are two things here, one is upgradation, and another is implementation. One is one-time investment, the other involves recurring costs. So many people make the upgradation, but they don’t use the equipment. That way, there is no recurring cost. So there is no actual implementation. It’s just for show.

The respondents also criticized the potential for unscrupulous practices with regard to regulatory approval and implementation since these largely depended only on the mere presence of the specified instrumentation and could also be secured through spurious documents. They revealed manufacturers’ anxieties in responding to the demands of the market. Also, notions about quality are articulated here, in a normative sense, as quality representing a philosophy that needs to be internalized and manifested in the everyday activities of the institution and its personnel rather than merely regarded as a set of technical procedures. Respondent 5 explains,

Quality is I feel, personally, a question of your own personal commitment and philosophy, you can have all the equipments and instrumentation and still make a rotten product, and you may not be actually using it. We test things carefully and then release it for our market, but the general thinking among firms is, there is pressure because you’ve sunk in so much money into all this, let’s do something and
get our product on to the market. One could also buy the equipment simply because our regulatory authority wouldn’t give you the approval in the first place without it.

Respondent 4 dwelt on some of the strategies used by firms to bypass protocols. These strategies usually involved skipping of certain tests or procedures in the expectation that these would not affect the final outcome of the product or be detected.

Let’s say I have to fulfill this big order and I have to do this particular test, but I’m desperate to deliver my order, so I say, let’s skip this test, take a chance, let’s not do this, anyway the product is coming out all right, we don’t do this, but some companies may do this. And their documents may be there. You have companies saying, okay, this is a big order; I’ll deliver this in 2 days…

These articulations also convey the frustration of the personnel in coping with the burden of additional protocols and tests, while ensuring timely delivery of orders, particularly in the light of their own commitment to scrupulously adhere to them. Respondent 4 asserted:

It gets difficult to deliver orders, see for antibiotics, it takes a minimum of ten days, at least seven days, with all these tests, and we comply with all that, we just can’t manipulate things like that, some firms do that…

The remarks made by Respondent 5 also underscored these anxieties to satisfy quality related demands while fulfilling the demands of their market. Though these narratives corroborate the usefulness of Schedule M protocols or even US-FDA protocols in monitoring parameters such as contamination levels or purity, the trope of “cost-benefit assessments” continually surfaces in their attempts to articulate whether such ‘incremental’ augmentation of product or process quality is justified in their particular context.

Raw materials’ testing takes one day, and then in process checks, then finished products, then packing, what ever you do it takes a minimum of four-five days. Even, in a US-FDA system, the procedure is broadly the same, it might be quicker. Say we might take a day with laboratory tests, they would do it in three-four hours using their latest equipment, our machine might make say 3 lakh tablets, their
machines might make say 15 lakh or 20 lakh tablets, but still, you can reduce the
time but you can’t totally eliminate it (the procedures). As far as requirements of
Schedule M are there, they’il say, this particular metal won’t do, you need to have
one of steel, their requirements are, any data you have, it should be able to be
audited, any changes you make in the data, it has to be recorded. They have
requirements, in terms of area, in terms of the finishing of the walls, surfaces etc.
The basic objective is to reduce the contamination in the drug. A U.S. FDA prepared
drug will definitely have less contamination. But see, for anything you do, there are
costs attached to it, so whether you really want to go in for it.

Similarly, in the case of Respondent 6:

See U.S. FDA gives product-wise approval. It’s not that the entire factory should be
approved. Suppose you want to export paracetamol, they will audit the product
facility for that. That would be approved by U.S. FDA.

Quality is also visualized here as an outcome of the level of autonomy given to the
quality control personnel in the organization to intervene and ensure compliance with
predetermined standards and their ability to negotiate with the top echelon in a typical firm.
What is interesting here is that rather than problematizing quality related issues in terms of
purely technical criteria\textsuperscript{106}, as one would typically expect, the statements of the respondents
repeatedly place the onus of compliance with standards largely on normative concerns and
values such as individual or organizational commitment, managerial styles, adequate
expertise of concerned personnel, market pressures etc. These statements are also indicative
of the snags encountered by a typical firm and its personnel in trying to faithfully replicate
the principles outlined in quality control or assurance manuals or GMP protocols dealing
with the industry. Again, these statements do not really challenge the utility or
philosophical principles of quality control and assurance but they critique the practices,
which have emerged around them. Thus, according to Respondent 5:

\textsuperscript{106} Although these are also dwelt upon by the respondents in the course of the chapter.
The first principle when you are talking of quality control is, the person heading the quality control department should be independent. How much freedom do you give him in terms of the authority to operate in a particular way and say no? In a quality manual, the person is supposed to report directly to the MD. What happens is, the cost of loss is too high. The financial in-charge or boss may say, what’s your problem, I’m there, and I’ll see to it, take care of it. As far as schedule M is concerned, you can do 200 things and show, you can follow the letter of the law, but are you following the spirit, that’s the question.

Likewise according to Respondent 6:
You need people with M.Sc., people who can understand all this. You need one person for the documentation itself. You need quality control and quality assurance. Quality control includes all these testing processes and testing of the final product. Quality assurance encompasses everything, it includes whether your raw material comes from reliable manufacturers, your whole procedure of handling it, the procedure of manufacturing it, how you handle complaints, how you handle dispatch. Whether it is as per the written procedures or not. For all this, our FDA requirement is that you should have an M.Sc graduate in Chemistry. All this is independent of automation.

From a sociological perspective, these remarks undoubtedly provide us with some simple examples of how, in the context of drug quality, the technical and normative dimensions are inextricably intermeshed. Undoubtedly, in the statements of these respondents and more importantly, in the context of their existential condition, as personnel employed in a charitable institution advocating drug quality in a fragmented industrial sector beset with market pressures and cut-throat competition, there is a clear recognition of such intermeshing.

Quality control and quality assurance manuals on the pharmaceutical industry do recognize quality as an outcome of a) tools and techniques involving statistical process control, b) putting a system in place, c) practices such as Kaizen, total productivity maintenance, just-in-time manufacturing, etc.) and d) the involvement of personnel at all levels of the hierarchy (Gharpure 2005). The Orange Guide defines quality as “the essential
nature of a thing and the totality of its attributes, which bears upon its fitness for its intended use.” Within this schema, quality in the pharmaceutical industry is broadly visualized as ‘an outcome of the continuous and integrated collective efforts put up by different arms of an organization, like men, machines, materials, methods and planning’. It involves dimensions such as infrastructural facilities, adherence to pharmacopoeia, use of standard operating procedures (SOPs), documentation and records, in-process testing, validation and education and training of personnel (ibid). Each of these dimensions is outlined in detail in the Good Manufacturing Practices manual used by firms in the sector. The central objective of these manuals and indeed the new Schedule M requirements pertaining to GMP protocols is ostensibly to ‘standardize’ firm-related practices and ultimately the quality of drugs manufactured in the sector.

However, the onus of tailoring these copiously laid down protocols, through the judicious use of the GMP manual and pharmacopoeia, in accordance with the local economic and political conditions, regulators’ requirements and specific organizational requirements, largely rests with the individual firm. As mentioned earlier in the present chapter, to provide one example, firms in India are permitted to formulate standard operating procedures in their own fashion and in the local language, provided these are in accordance with the guidelines outlined in the Schedule M protocols. Thus Respondent 6 asserted:

These SOPs may also be translated in the local language, since they are meant for the workers. These are generated in-house by respective people. I would generate for production, he would generate for quality control. There are some broad guidelines, which you need to follow, but you can generate it in your own way.
Moreover, variations among firms in terms of the level of automation, the extent of
documentation they carry out, their procedures are also permitted if these are shown to be in
accordance with required regulatory protocols. The respondent added:

The process that is followed should match the broad guidelines as per their
(regulators’) requirement. There are two things that are constantly followed,
validation and calibration. Validation is showing what you are following and
calibration involves accuracy of your parameters when you follow some procedure,
for manufacturing and testing.

Respondent 5 remarked:

In the case of SOPs, if two manufacturing units are there and both of them have
Schedule M certification, having similar equipment and manufacturing the same
drug, their SOPs will still have variation. Variation is according to what is the
appropriate procedure you think, what is needed. It’s just that, if suppose in your
firm, you follow a procedure, you stick to that, you have to justify why you are
following that. The process that you follow, if it can be validated and you
consistently get good results and similar quality drugs in your final product, you can
justify it and you can do it your own way. The same thing holds for the other firm if
he (the owner), is getting the same results by doing it his way. Why should he follow
you or vice versa?

The respondent, however, also added:

But even if you set your process in a particular way, there is always going to be
some amount of variation or spill, because in each batch, no matter however well
you think you have processed it, some variation is going to be there. That’s where
your skills and expertise counts, how you manage this variation. It’s like a
mechanic, who by hearing the sound of the machine, knows what the problem is,
that’s his skill, similarly how you tackle these variations, that’s where your
knowledge counts.

The respondents repeatedly emphasized that similar product quality could be
obtained and validated, independent of firm-level differences in certain aspects like SOPs,
procedures, methods of documentation and degree of automation. In the case of aspects like
reduction in contamination and minimization of human error, the respondents conceded that
protocols such as those instituted by the US-FDA did have an advantage over the Indian
Schedule M related protocols. The person who comes in to do it, mostly they’ve never done it before. The problem is I don’t think our FDA officials themselves even understand half of the rules they’ve specified. We have a very poor impression of our FDA. The kind of people we interact with half the time, their understanding level, their knowledge, it looks like some kind of clerical person, the kind of queries they pose, why did you write IP as I.P. instead of writing IP, of course this is taking it to a very ridiculous level. But these are the levels of objection they raise. The DCGI might understand all the protocols of Schedule M, who knows, (laughs), but the inspectors who come; they however, paradoxically enough, variations occurring in a batch, were constructed as an inevitable part of the manufacturing process rather than the above-mentioned firm-level differences.

Such a construction, may in part, stem from their anxieties over the competition from larger players in the market, since the Trust, for the most part, functions like a typical small scale firm. Large firms in the Indian pharmaceutical industry market their products by emphasizing on the certification they possess from regulatory bodies like the U.S.-FDA and UK MCA, claiming such certification to be an indicator of the superior quality of their products and their manufacturing process in terms of adherence to protocols, tests, documentation and use of automated technology.

The competence of Indian regulatory officials in terms of their assessment of quality related issues also came in for scathing criticism from the respondents. Regulatory officials were perceived as novices and lacking proper knowledge about processes or procedures, bureaucratic and corrupt. The impression was that a proper insight into the implementation aspect of the Schedule M protocols was absent among field-level officials of the FDA, who visited the firms to enforce and ensure compliance. In this context, Respondent 4, in an indignant vein, commented:

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\[^{107}\text{See page 28 of the present chapter.}\]
are the ones who are supposed to be implementing these things. I don’t think they know what they are dealing with.

The rationale for stringent implementation of the space-related requirements, infrastructure and instrumentation, all integral aspects of the Schedule M protocols, without adequate assessment of their necessity or usefulness in terms of augmenting work environment or efficiency of the manufacturing process was also questioned. Respondent 5 remarked:

See there are some space-related requirements. The inspector, who came, said, ‘measure the height of the window from the floor’, it was done with a tape, then he said, its 3ft 6inches, the requirement is 3ft. Your application may not be passed. So I asked, how does it matter, the fellows inside should be able to get proper light and air, anyway you have the air conditioner. But he was very adamant. He said do the leveling. We have some 40 windows. We had to do these things. So, some of their requirements don’t really make sense.

The observations made by Respondent 6 also reinforce their ire against officials, who insisted on going by the manual in terms of instrumentation requirements. The argument here was that such an approach was valid only in the case of those requirements which contributed to process or product quality augmentation in actual terms. They go to these other firms and pick up some ideas from there. Like, this room should have all these things. Do you have all this? The inspector came and saw our granulation room. He said air conditioner is required. I’m telling him, we have a dryer also there. So the air conditioner cannot work. He asked how your people can work in this forty degrees temperature. I’m telling him, it’s not coming to forty degrees. See, when heat is also there, from the dryer, how do you use air conditioner? But he didn’t agree. He said I cannot pass it. It’s mentioned in the Schedule M that you should have all this. So the result is we spent 1.5 lakh rupees and we had to comply. But what is the purpose? That is important. See, I can have air conditioner. But I needn’t switch it on. It can be there just for show.

See, there are certain things about Schedule M that are reasonable and required. Like having the microbiology lab in-house is good, these tests are required, if you are really serious about quality. The requirements related to stability, if you follow it properly at every step, it really helps to maintain quality.
In yet another instance recounted by Respondent 5 to demonstrate the hard line approach of regulatory officials, the thrust of his argument pertained to how the lack of official expertise or interpretation of the protocols prevented a ‘rational’ discussion and negotiation on what kind of variation in terms of requirements was feasible or valid without the jettisoning of quality-related concerns.

As far as water systems go, now you need reverse osmosis. But there are certain things like, when I went to our FDA office for the approval, they said reverse osmosis is required, but when I asked why it’s required, they are not able to explain. They wanted this whole circulation system where the hot water keeps circulating at eighty degrees throughout the system, that’s very costly because you have to keep heating water throughout the day and it has to circulate till the user point, may be ten-fifteen feet away, so you need a motor and things like that. So we tried to explain that it’s a very costly thing, we don’t need it, it’s not really going to lower quality, because we don’t use liquids and that’s when it’s really required, but they wouldn’t hear any of our explanations. You need it and that’s it. Then what we did was, we came up with our design and specification, that would suit us, now what we designed also leads to circulation of good quality water, and as long as we are able to show that, it should be fine, but some inspector comes along and doesn’t agree with us, and says no you have to have that particular system that’s mentioned and then what do you do? For liquids, okay, it’s a must, but not for what we do.

The involvement of the respondents with respect to quality-related issues in the present context is undoubtedly of a more engaged nature. There is a constant questioning of how different standards pertaining to quality ought to be constructed or interpreted. The normative concerns expressed by the respondents are also indicative of the larger tensions existing between these groups, regulators and the Trust’s personnel, over expertise. While the Trust personnel raise questions over the expert knowledge of the regulators, their construction and interpretations of the protocols, the regulators on their part seem to be questioning the legitimacy of the Trust’s personnel to raise objections to their interpretations.

But that’s the thing with inspectors. You have to put up with whatever they say. You argue, you lose. They all have this bureaucratic mindset. You just have to keep
noting whatever objections they have raised. Earlier, we used to argue, but now we listen silently. It’s not worth the trouble caused. These inspectors who come, they have a bureaucratic mindset. If it is 25, then it has to be 25, they don’t understand that there can be variation, with a valid reason.

In this context, Respondent 4 added:

Our FDA system sometimes works on the basis of bribes. None of the other firms will admit or tell you this. But this time, anyway, the gentleman we dealt with, he knew the subject somewhat, what he was doing. In our case, they’ve approved our earlier product also. But before our process of retesting, reprocessing, was in place (for Schedule M), they gave us new product approval, before we could do test batches and so on. So proper continuity is not there.

The respondents also outlined the glitches they encountered in their everyday practices in the context of compliance with Schedule M. Automation and even going strictly by GMP protocols or pharmacopoeia was perceived as unhelpful in the case of manufacturing processes like granulation or preparation of excipients, which required manual handling of the material and tinkering around with the process. In this context, the respondents outlined how similar were deployed in large firms in India. Respondent 6 elaborated:

See as far as granulation process is concerned, granules have to be actually checked by hand, to check whether it is done properly, but Schedule M would not allow that, on grounds of contamination. As far as process is concerned, it’s mainly whether things are done as specified, cleanliness is being maintained. In the case of granulation, I am telling you, same older methods are used inspite of automation, still the same thing continues everywhere inspite of automation,, even if you go to any big unit or any other formulation unit. When I was with a big company in Ahmedabad, there also it was there. Whatever it is, in the granulation phase you have to use your hands, otherwise, fine granules, hard granules, how to get it? If you take wet granules, by taking it out, and seeing them, I can say, add one more litre of water. Once you do that, you pass it through the multi-mill; you immediately find the granules are ready. With granulation process, it’s not fixed, it’s not like you need 5 litres of water, sometimes it may require 4 litres, sometimes 7 litres, so that manipulation is going to be there. Once you do the granulation then, then the process gets done quickly. There automation is just fine. But initially, whether it’s okay or not okay, in the mixing stage, for that you need the older methods. Here I am able to do that. With closed machine, how I’m going to do this?
Interestingly, automation is therefore not perceived as an adequate substitute for skill and expertise of work-force, though with regard to certain processes, the respondents do regard it as advantageous in terms of quelling labour related issues. The respondent added:

Automation is done for making production process fast but you need some typical technical people, who have hands-on experience, like that old worker I told about, you need, to check the consistency of the material. Then only it can be decided. It’s like making sweets, with sugar syrup. Unless you check the consistency with the hand, you wouldn’t really know. The same funda applies here.

The thrust of these arguments is that such manual tinkering with the manufacturing process does not in any way reduce from the quality of the final product.

What we do here, for excipients, its paste, starch paste. It’s a binder. And starch paste making is also an art. It requires uniform heating etc. Starch paste, if you put it in a closed vessel and think, it’s going to be done automatically, it won’t be done. It might get charred also. If you put it in a closed vessel, it’s not going to work. In certain cases, you have to use our own way of manufacturing, but ultimate motto is quality. But in automation, the advantage is that labour problem is reduced.

These arguments, in a sense, are posited as a counterpoint to the principles of Schedule M and even those of international regulatory bodies, which emphasize not only on consistency in the final product but of the manufacturing process itself.

The respondents are nevertheless in agreement about the larger administrative advantages offered by automated programmes like SAP, which are used to control the process of production in large firms. These are essentially used by Indian firms, which have acquired approval of international regulatory agencies for certain products and which use these programmes for the export market. These programmes are used to facilitate greater managerial control of the production process. Respondent 5 elaborates:

SAP is a programme dealing with the automation of the production system; it is a programme, where if you have multi-units, just by sitting in one place, you can know anything about the production status in the company. Production position,
finance position, raw materials, in-stock position etc. There are different programmes like this used by different firms. Basically the idea is this, everybody enters their data from their location, regarding production, quality etc, and it goes to a central server and any facts or decision the management wants can be accessed. Your database is ready; any fact about the company is ready on the finger tips.

The respondents are, however, also quick to point out that the incorporation of such programmes in the production process, even in large firms, does not necessarily lead to increased dependence on technology rather than skills of personnel, since these personnel from different units, concerned with process monitoring (manufacturing), quality control, packaging etc are expected to manually enter the data into the system from their end. The advantage that these programmes are perceived to confer is its capacity to integrate and synthesize all this varied data and provide an overall and systematic account of the activities of the firm to the management. It may be noted that different kinds of programmes are used by different firms and they are customized to the needs of the organization.

The Trust has also utilized one such programme in order to keep track of its financial activities. It plans to integrate this data with the manufacturing and quality control related data in due course. Respondent 9 explained:

We have MPS, it basically does the accounting part of it, we took a tally and we have tried to integrate it with our production part also, the aim is that we ultimately integrate it back with our process and laboratory part also. It’s called financial accounting system, so you know about your stock, your debtors, the bill is entered, as soon as its entered it gets debited in the debtors ledger, it gets debited in stock, your balance sheet gets ready instantly, so if I want to know after March end what is sales, debtor’s list, what is the raw material stock position, everything comes in a bunch, It gets more complicated if you have multi-locational plants with multi-products. It’s just the level of complication that the programme can accommodate. It’s not that you are not dependent on individuals and more dependent on technology, because every individual has to enter the data. In manual mode, if I prepare a bill, I have to transfer it to a ledger, transfer it to stock; in automatic mode, if I just enter the bill in the system; everything gets taken care of automatically. One entry takes care of 4 things. In the last 15 years, we have been running everything with just me around. I take care of all our accounting, our balance sheet, dispatch,
billing etc. It’s just multi-tasking where one person takes care of everything. In terms of financial package, that’s the only skill that’s required.

However, in this context, the respondents also reflected on the change in skill requirements for personnel manning automated systems. Their understanding was that in production systems, which were highly automated, skill requirements for the average machine operator in the manufacturing unit tended to decrease, since the individual was merely expected to fulfill tasks such as switching the machine on and off and keeping track of any deviations in parameters, though this latter function was equally the responsibility of the supervisory level personnel. The operator was not expected to shoulder the responsibility for the maintenance of the machines. However, with regard to maintenance and trouble-shooting in the production unit as a whole, including quality control, the skill requirements and expertise were generally of a high level and the individual in charge was expected not only to maintain the machines but also ensure smooth functioning of all the linkages in the system. Respondent 5 elaborated:

In highly automated systems, it becomes easy for the operator, he just has to press the button to start or stop the machine and he doesn’t know the nitty gritty, but for the person who is maintaining it, integrating it, it becomes correspondingly difficult, his knowledge base has to go up. Earlier he would have to just manage the machines. Now he has to manage all the linkages too. So there the knowledge base has to go up. You can’t have a normal fitter. Repairing becomes very difficult because you have to call in some one who knows the whole system, maybe the manufacturer.

Respondent 6 outlines the differences between manual and automated technology in the context of the packaging related activities carried out in the Trust.

Automation in packaging means the machine does the folding, pasting and punching of the carton or box. Also, in the case of cartons, it will strap it, pack it with the strips and throw it out. It is really fast. If you want to produce 5000-6000 boxes per day, it is impossible to do it in semi-automated mode or manually. And you cannot lift the required 100 kg, 200 kg paper roll manually. Imagine it runs at about 70-75
metres per minute. How fast it’s done! There is efficiency in cutting, folding and measurement. Here what we do for the cartons and boxes and packing the strips, this is manual. You can see these lines. In imported boxes, you won’t feel these lines.

The respondent also highlights another important fact, which is useful to our understanding of quality related contestations in the sector. In the Indian pharmaceutical industry, majority or the large firms outsource drugs from small and medium scale firms through contract manufacturing and then sell it in the local market. The automated technology in their production unit is generally used to produce drugs for the export market and with an eye on international quality certification. However, in order to retain their brand value and reputation in the market, they send their manufacturing and quality control personnel to these units in order to supervise them and ensure that these products match their specifications. Thus the vast majority of the drugs sold by large firms in the local market are actually produced by these small and medium scale firms with manual semi-automated technology.

In the course of field work undertaken for the present study, interviews with managerial-level personnel responsible for the overseeing of manufacturing activities in seven large firms, revealed how these firms equated sophisticated equipment at their shop floor, their state-of-the-art drug testing instruments and their compliance with international manufacturing protocols with ‘better’ quality. Also, the high prices of their drugs in contrast to the prices charged by small and medium scale firms in the local market were felt to be justified given the steep costs of such equipment and instrumentation. The respondent’s articulations attempt to uncover these inconsistencies with respect to large firms’ claims of producing ‘better quality’ drugs, especially in the context of the Indian market, though he
concedes that large firms are particular about providing requisite training to these small players and ensuring compliance.

With regard to the small players, even big players are depending upon small units. It depends upon for whom you are manufacturing. Whether you are carrying out these tests. Big players are careful since if something is rejected, their name in the market will be spoilt. If they insist on following a particular procedure, then the small firms manufacturing for them will have to comply. They actually outsource from these firms and then sell to local market. For export, they manufacture in their own automated facility and then they market it abroad. In big firms, they send their production and quality people to these small players, who train them. They’ll train them to do it in their own way. They have a right to reject the material. Often they reject it also.

The Trust as a policy does not employ workers on contract. In addition to the managing trustee and the seven supervisory and managerial personnel, around thirteen workers are employed in the production plant. Majority of these workers are utilized in the packaging section at a time. In the last two years, the trust has not employed any additional workers, inspite of the fact that it has been unable to meet its sales orders a few times due to paucity of the work-force since there is no consistency in terms of market demand for its products. However, Schedule M protocols do not directly specify any need for increase in work force if compliance can be carried out with existing work force. As mentioned earlier, the Standard Operating Practices (SOPs) are explained in the local language and in detail to the workers, since they are questioned in detail about the various manufacturing processes during inspections by regulatory officials.

In Schedule M inspection, they will ask questions to the workers, what he is saying, why is he saying, he should be able to explain that. Give the justification for that. They don’t ask the supervisor. He should be able to read, understand and explain the logic of the SOP, whatever he is doing. Roughly our sales turnover is around 3 crore. But we feel, we have the scope for growth. Sometimes it happens that we have a large order but we are not able to produce it. But that is a temporary phase. It doesn’t happen all the time. So we cannot increase the no. of persons or workers just because of that.
Unlike the fragmentation of skills or expertise, which happens in large firms, within the Trust, as in the case of small scale firms in general, all the workers are usually entrusted with a variety of tasks, including operating machines, assisting with manufacturing processes and packaging. This is because, unlike large firms, the miniscule size of the workforce does not really enable fragmentation of skills or expertise. The respondent’s articulations also highlight the “hands-on” experience and tacit skills possessed by the workforce, many of whom are less qualified, education-wise, in comparison to their counterparts in large firms. The respondent’s remarks also highlight the significance of the workers’ role and expertise in understanding the manufacturing process, compliance with protocols and augmentation of product quality in less automated units.

Though our operator is good, everybody (workers) is capable of doing any job. We talk about theory, but they know the practice, they have a lot of experience. Our institution does not believe in hiring on contract. Workers do operating work, helping with production, and packing, finished godown packing also. The workers are all 10th pass, eighth pass etc. One of the workers in our organization has studied only till the third standard. But he can always tell if the capsule has been made properly or not, which even I can’t tell sometimes. He has hands-on experience of many years and is one of our oldest workers. They work in shifts depending upon priority and work load. When there is production going on in this general section, the production in the Betalactum unit will not be there.

However, notwithstanding the importance of the workers’ tacit skills in these firms, the respondent’s remarks also point to their gradual erosion in a changing shop floor, especially in large firms, where manufacturing processes have to be specified in minute detail by supervisory and quality control personnel, thus placing curbs on the independence of the worker and the opportunities to exercise his tacit skills and judgement. Such fragmenting of the production process is in accordance with the demands placed by the Schedule M and other international regulatory protocols. Glitches related to the production
process are handled within the Trust itself, since the manufacturing process is largely semi-automated. The Trust also relies on the acumen and expertise of its workers to resolve these issues. The respondent also highlights how in large firms, due to sophisticated machinery and their complicated network of linkages, coupled with the fragmentation of skills, their firm personnel seek the assistance of the manufacturer of the machines or instruments in resolving problems related to such equipment.

Regarding the size of the work-force at the work station, it depends upon what is the product that you are making and the size of the factory. But now, also, the worker doesn’t have any independence, since the processes are specified in minute detail by the supervisor, by the quality control. In our case we have a person, an operator, who is not even tenth pass, but who has a knack for repairing and maintaining things, he understands the process well and also manages all the machines. In our firm, if there are any glitches, we manage it ourselves. In big companies, one computer engineer will be there, he will manage minor glitches, for major problems you have call the manufacturer. Though the workforce is reduced there but you need supervisiorial backup. If there is a problem who’ll handle it? Earlier the person would come with a fitter to repair the machine, but now skills are changing, he has to be able to understand the linkages in production line. Since the machine is managing everything, naturally workforce is reduced. That’s what’s happening in these firms at the shop floor level.

However, packaging activities are perceived as manpower intensive in many firms in the sector. These activities are usually carried out by women due to notions about their having the necessary patience and “nimble fingers” to perform these tasks. For the most part, automation as a strategy to improve the production process was justified by the respondents on grounds of their being a “one-time investment” and providing relief from unionization and labour related problems. Interestingly, even as the respondents recognized the worth of the tacit skills of the workers in their organization, they also attempted to illustrate, through different examples, how sophisticated or automated machinery did help in terms of improvements in the quality of their products. Respondent 5 explained:
Manpower is still needed. The packing part of it is still labour intensive in many firms. Usually you have women doing it. You need a lot of patience for packaging and the general understanding is that women do it better. The major portion of workers in the pharmaceutical industry today, is in the packing part of it. It’s easier to manage machines because with machines it’s a one-time investment. For instance, we have a machine in our firm which has replaced four people. This machine is for filling in the material in capsules, it’s a capsule loader. Earlier we needed four or five people to do it. Then we got it in 1995-96, with that, there has been an improvement in production. It becomes faster, more efficient; you need just one person or maximum two people to operate the machine. Also, the requirements change. You know, in small scale sector, capsules are graded, first category, second category, third category and so on. Generally the third category rates are lower. Of course, there are only minor variations in these categories. But when you are using this machine, the quality of the capsules you make, that goes up. So those kinds of changes we have made, according to our specifications. With manpower, it’s an increasing cost, you are paying someone something today, you have to pay more in future, holidays and you have to factor in a lot of other things. Then there are labour problems, that’s one of the basic reasons for automation.

At the level of the firm or organization, the Schedule M inspection or audit is largely an internal affair between the regulators and the firms, involving negotiations and compromises on how the data should be interpreted and on which quality criteria should be regarded as valid. However, the Schedule M protocols are also perceived as externally developed standards or standards emanating from protocols developed by other agencies like the World Health Organization or the United States Food and Drug Administration (US-FDA), which have been edited and adjusted to fit local circumstances. Respondent 4 elaborated:

Our Schedule M is supposedly inspired by WHO GMP and US FDA. In certain places, word to word they have copied. US FDA is also creating entry barriers too strong for you to overcome. Like for this bulk drug company here that was trying for US-FDA, they said, you have to get some particular equipment from some American company, you can’t use any other brand. But also because more of our drugs are entering the European and American market. They don’t want some regular Third World stuff, so they want to make it as stringent as possible. They want to reassure their citizens that even if these foreign companies are coming in, they are doing everything possible to ensure their safety. Also, there is now this move towards harmonization. Their philosophy is, if there is uniformity in standards, it is easy to
regulate. Now if you have a WHO-GMP certification, it becomes relatively easier to get a U.S.-FDA certification. Or even regulatory approval from Europe.

The articulations of Respondent 6 seek to underscore the differences between the protocols instituted by Schedule M and those required by international regulatory bodies in terms of instrumentation.

In validation, if you are saying, I am doing these things, you have to justify why you are doing these things. Calibration is related to improvement, if it says 2 grams, does it really mean 2 grams, which is calibration. If you have equipment, this equipment should be certified by the government of India. The variation produced by the equipment should within a particular specified range. That again is calibration. Here we have machines purchased in 1993-94. And for the quality testing, the IV-R, that is the spectrophotometer, also was purchased recently. IR came from Germany, now we are planning for HPLC also, High Pressure Liquid chromatography, in order to test the purity, the content. HPLC is more exact, it gives detailed graphs, it gives the impurity profile in a detailed way with each active ingredient and even the excipients also. That is a must for international quality certification. Soon Schedule M will also require the HPLC. I think that is what they must be planning. What will happen is that one fine morning it will come and then we will have to purchase it. This may be a plan to eliminate small players from the business, if you raise the bar in terms of quality standards and procedural specifications, naturally they will not be able to follow and only medium scale and large will remain in the business. IDMA is trying to do something about this but sometimes say I have introduced a new machine for some process, there is the tendency to give money to the FDA people here so that my machine will be sold.

These seemingly routine negotiations over protocols related to infrastructure, instrumentation and manufacturing processes are perceived as having larger politico-economic implications. The progressively stringent Schedule M standards and particularly the global shift towards harmonization of standards, advocated by international bodies like the ICH and regulatory agencies like the US-FDA and the UK-MCA, are therefore viewed with trepidation and as potentially capable of creating entry barriers for small and medium firms using the agenda of better quality.
At the same time, the respondents are not dismissive about the protocols specified by these international certification agencies and do recognize their potential in terms of augmentation of precision in the manufacturing process and purity of the drug, enhancing the expertise of the personnel, reduction in strength of work-force, consistency in the manufacturing process and product, reduction in time taken to manufacture a typical batch and reduction of manufacturing-related errors. Respondent 5 elaborated:

All these international quality certification systems, they reduce time and the possibility of error. At the work station, because of automation, at the level of the workers, it reduces strength of workforce, but at the level of the quality control personnel and supervisory level, the level of expertise, that will go up. Their principle is, in any process, you use as many people as you want, as less people as you want, you prove to me that the process you are producing will produce a consistent product according to our requirements over the years. These chaps they say, if you are saying that this is consistent, you show at every stage how it is consistent. All over the world, whether it is the European system or the American system, the focus is on the process. If your process is validated, automatically the quality of your product becomes good, that’s their understanding. Since, you’re conforming at various stages. In fact, in the U.K., they don’t check your final product, they check your process. That’s all fine, but if you tell me that such a drug is going to be therapeutically more efficacious than say what we produce, that’s not really accurate.

In the words of Respondent 6:

US-FDA basic premise is that anything you do, any variation that is there, should be capable of being checked, should be documented, there should be a log of, say at this time, there was this variation, and there is this record of that. What happens in U.S.-FDA type of compliance, is, suppose you do a dissolution test, you attach it to a computer and a printer, so the system automatically gives you an idea of what has been recorded once the equipment begins functioning. In Schedule M also you need to do this; deviation in parameters can be more here, you can do it manually, provided you have a log of all the details.

These declarations, however, seem inconsistent, given their ire over some of these very same issues in the context of Schedule M protocols. This inconsistency may be
explained in part in the context of their perceptions\textsuperscript{108} that the Schedule M protocols have been borrowed liberally from the protocols constituted by these above-mentioned international bodies, but in an unsystematic and arbitrary fashion, lack proper rationale with respect to certain specifications and are implemented by incompetent or ignorant officials in piecemeal and frequently illogical ways.

According to the respondents, one of the key differences between Schedule M and these international regulatory protocols is the space for deviation in parameters. While the levels of precision demanded in terms of parameters in international regulatory protocols, governing the manufacturing process are high, usually requiring sophisticated instrumentation, in Schedule M, these are relatively less and are permitted to be performed manually, provided they are documented and capable of validation. What is also noteworthy here is that though these international protocols come in for praise with respect to the aspects mentioned above, the respondents do not concede that these improvements translate into better quality in terms of added therapeutic efficacy of the drug.

Concerns about what really constitutes quality are also articulated in the context of issues related to sampling and statistics. The argument here is that quality can never be understood or defined in purely statistical terms since theoretically there is always the probability of a 0.01 error. Respondent 5 explained:

\textit{See there are also these other problems related to sampling and statistics. Finally what is quality? Any procedure or validation, if you see, if you mix up these things in such and such proportion, you’ll get a product with this particular percentage of purity, but if you see, there is only a 99.9 percentage probability of that happening. There is always this 0.1 percentage chance that it may not happen. Is it that your drug will not be of good quality? Even in every 100 batches, one of them can have variation.}

\textsuperscript{108} These have been dealt with elaborately in the earlier parts of this section.
In a similar vein, Respondent 6 echoed:

If you see the case of tablets, the smallest tablet that we make is around 120 mg. Out of that the active ingredient in many cases is 4-5 milligrams, so how much percentage of the active ingredient do you get? It’s around 3-4 per cent. Now in such a case, the chances of making a tablet without the active ingredient are always there. When you do the mixing and you follow procedures, you try to ensure, but still, there is always a statistical probability of getting a tablet without it. But there are procedures, methods and processes, you validate and you try to reduce the probability, the chance, of that happening.

**Discussion and Summary**

The larger issue here, and one more relevant to the present study, is that there is evidently a fragmenting and digitizing of the notion of quality or the investing of a drug with quantifiable attributes. These quantifiable attributes, which are advocated by international regulatory bodies as part of their agenda of uniformity and standardization, and to a relatively lesser extent by Indian Schedule M protocols, are embodied through standard operating practices and the emphasis on augmentation of precision in the manufacturing process, sometimes through the use of sophisticated technology. However, such quantification is not very informative on what are the precise or incremental therapeutic benefits accrued by adherence to these protocols in terms of the final product, if quality is also understood to subsume therapeutic efficacy.

The implication here seems to be merely that such a drug, whose attributes can be quantified and validated and which is produced through a stringently verified manufacturing process, accredited by an international regulatory body, can yield therapeutic benefits in terms of being a safe product, with the predetermined levels of purity and which acts in ways in which it is expected to act. But whether such a product is of superior quality in
contrast to a drug produced through stringent and scrupulous adherence to Schedule M protocols in terms of actual therapeutic efficacy remains a subject for debate.

In the context of manufacturing, there is clearly a fragmentation of the drug in terms of its technical attributes such as stability, potency, efficacy, purity, etc. However, the qualification of the drugs in this context is articulated in terms of norms such as regulators’ professional expertise, the ‘appropriateness’ of the protocols in terms of augmenting therapeutic efficacy, organizational commitment etc. Additionally, the qualification of these drugs is also sought to be understood in terms of larger concerns like the harmonization of protocols and the creation of entry barriers for small firms.

Some of these issues on the qualification of drugs during the stage of manufacturing and commercial production would be examined in further detail and on a larger canvas in terms of understanding the contestations between the firms, regulatory bodies and health activists on these issues in Chapter 7 of the thesis.