Concept Design for Establishing an Eco-Friendly Pharmaceutical Production Facility in Malta

The authors discuss the concept design of a versatile, sustainable, small-scale facility in Malta that conforms to the European Union’s current good manufacturing practices.

Methods

A fixed capital investment (FCI) plan has been drawn up, which forms part of the second phase of this research. FCI was identified using the “detailed-item estimate” method (6). A list of items required for the planned facility was established through site visits and as part of the design criteria. This exercise was then carried out by scrutinizing online product brochures and requesting quotations from corresponding local suppliers. Careful planning was given to the construction, main process equipment, and laboratory equipment, as well as utilities, such as heating ventilation air conditioning (HVAC), and systems for water purification, steam, vacuum, dust collection, and compressed air. The aforementioned considerations are the basic requirements for a start-up and require the most extensive capital investment.

The third phase consisted of estimating the number of full-time personnel required to run the facility. Average wage structure was gathered from a local pharmaceutical company. The annual operational costs were estimated, taking into account bank loan interests without security, depreciation expenses according to local legislation (7), and other expenses gained according to local unit costs, and other expenses. Average wages in line with local unit costs, and other expenses gained according to local conditions were estimated. Annual operational costs were estimated, taking into account bank loan interests without security, depreciation expenses according to local legislation (7), and other expenses gained according to local conditions were estimated. The third phase consisted of estimating the number of full-time personnel required to run the facility.
The facility under consideration is a stand-alone, multi-story facility that could produce several non-sterile OSD products, except drugs of abuse and cytotoxic drugs. Its façade is planned to accommodate for the installation of integrated photovoltaic technology. The facility is planned to be south-facing to optimize natural lighting for the auxiliary area.

It is envisaged that the facility will make use of approximately 4700 m$^2$ of land, with a floor area of approximately 8000 m$^2$ spanning four separate levels with interacting industrial lifts. Waste and solvent rooms as well as an electricity substation were planned separately from the facility to minimize safety risks. An underground parking area can also be considered for the facility.

The ground floor (see Figure 1), with a height equivalent to two stories, will include the warehouse that includes a dispensing area containing a down-flow booth using extract technology. The notion behind having a dispensing area on the ground floor is to reduce the waste flowing into the first and second level.
The first floor (see Figure 2) will be for the packaging of OSD, with locked storage for the printed packaging material. It will have direct access to the lift from the dispensing area. The plans accommodate for eight blister lines and/or bottling lines. It was taken into consideration that both primary and secondary packaging processes will be carried out in ISO Class 8 areas. This floor will also accommodate a microbiology and chemistry laboratory. Through the latter, one can access the stability chambers.

The second floor (see Figure 3), with height equivalent to two stories, will host the actual tableting process, including granulation, compression, and coating, which are maintained at ISO Class 8 specifications. A technical corridor runs around the perimeter of this level to enable technical support and maintenance of the equipment. The rationale behind having these processes on the uppermost level is that they will require extensive use of utilities and services. By putting them on the top level, savings are achieved in duct work installation, and air system complexity is minimized (8). Shafts for these processes can be constructed to provide to this level through the ceiling and allow the other shafts to supply the ground and first floors. There is also a research and development laboratory on this level, with an interacting samples room.
A utility and services space is on the uppermost area of this unit, which will include services for HVAC, vacuum, steam, water purification, dust collection, and compressed air. This space will be roofed over to protect the equipment and pipes from harsh weather.

Plans for the various floors take into consideration unidirectional flow of personnel, material, and waste to prevent cross-contamination (9). Standard operating procedures (SOPs) will form part of a quality system to regulate GMP activities within the facility.
Pressure cascade system

The pressure cascade system is managed by the HVAC system, which provides air as necessary to create pressure. Spaces that should remain cleaner than their adjacent areas must have a higher positive pressure (8). Processing rooms have lower pressure than the clean corridor, so that the higher pressure in the corridor helps in leaving contaminants in their respective suites and prevents their transfer through the corridor. The concept of the pressure cascade system for the second level of the facility is depicted in Figure 3.

Bubble airlocks were designed to act as transitions between the unclassified and classified zones. Bubble airlocks usually have higher pressures than the adjacent areas, to keep any contaminants in their area (10). Prior to entering any lift in the production area, airlocks (AL) were also designed so as to isolate any possible contamination coming from the warehouse, which is essentially an unclassified area.

Figure 4: Pie chart depicting the breakdown of fixed capital investment.

Fixed capital investment

The capital expenditure, worked in a detailed-cost estimation, amounted to nearly €13.4 million. Figure 4 shows a breakdown of the capital cost.

Consideration was given to items that enhance sustainability, such as a building integrated photovoltaic system for the façade and photovoltaic cells on the roof, which are feasible renewable energy sources for Malta’s subtropical-Mediterranean climate. Sensors and LEDs for the auxiliary area, a reliable building management system, and building insulation were also taken into account.

Operational costs

A GMP pharmaceutical facility should have an adequate number of well-trained and qualified human resources (11). There will be 36 full-time employees engaged in the facility, 15 of whom will be designated in production roles. The remaining staff will be employed in non-production positions, including four personnel in quality and seven working in laboratories. Their total salary cost (including national insurance according to Maltese legislation) is just over €1 million.

Operational costs of this facility to hypothetically produce 100 million OSD over the year 2015 were estimated to exceed €4 million. Included in this figure is the depreciation cost. Depreciation is the measure of the decreasing cost of property over time, which is seen as an expense (12). According to Maltese law, deductions for wear and tear should be calculated in a straight-line method over a minimum number of years (7).

Energy saving measures taken into account for this facility, are estimated to enhance the bottom line by more than €70,000. Figure 5 shows a detailed breakdown of the operational costs.

Figure 5: Pie chart illustrating breakdown of running costs.

Environmental benefits

In today’s world, priority is given to safeguarding the environment in response to global warming. Large industries are wary of their carbon footprint, not only because of concern for the environment, but also to uphold the reputation of the company among the general public. “Green” issues to be tackled to boost a company’s environmental credentials include waste management, recycling, energy reduction, and conservation (13). Malta aims to encourage good practices, such as making optimal use of natural resources in an environmentally friendly manner (i.e., least possible usage and maximum re-usage) (14). The proposed facility will minimize carbon footprint by embracing renewable (i.e., solar) energy, which will also help the enterprise financially by reducing operational costs (15).

Efficient and sensible use of land and sea are crucial factors in the macroeconomic and social development of Malta given the high population density, space requirements for industry, and the land-intensive needs of waste disposal and shipping (16). Bearing in mind that there are no imposed height restrictions in industrial parks, a vertical facility will safeguard the relatively limited land space.
Conclusion
Local stakeholders believe that a small-scale OSD facility can meet the needs of a potential niche sector for the pharmaceutical industry in Malta, apart from biotechnology that will hopefully flourish on the island. It is imperative to note that investing in efficient infrastructures will contribute to the local growth of the pharmaceutical industry, thus having a positive effect on the biotechnology industry.

References
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