Considerations in Designing an Excipient Dispensary

An IEDCO White Paper

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Industrial Equipment & Design Company

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Introduction

Many existing pharmaceutical facilities deal with their excipient dispensing in a very manual way, i.e. scooping or pouring material from drums or sacks into a drum or other IBC on a scale. Obviously, this leaves a great deal to be desired from both an ergonomic and containment standpoint, not to mention potential product quality, batch accuracy and documentation issues.

Designing a modern, automated dispensary is very desirable and offers many advantages, especially in the context of a new facility that is relatively unrestrained by existing architecture and validation considerations. However, designing such a dispensary is not as easy and straight forward as it may initially seem.

Designing a dispensary is a process. There is no one, right way and every facility has its own set of interests, priorities, space constraints and personal and personnel preferences. For this reason, designing the dispensary is a process that must begin by understanding and defining all of these variables so that the designer can incorporate and/or address all of them into the initial conceptual proposal.

This paper has been written as a general reference and example of the considerations that might go into the design of such a facility. It may be a useful tool for discussion in developing a conceptual model for your dispensary.

Some significant considerations include the following:

- Relative Location to Warehouse
- Raw Ingredient Container(s)
- Type of IBC
- Weighing and Checkweighing
- To Sieve or Not to Sieve
- Type of Batch Feeder
- How to Transfer the Excipient
- Dedicated or Multi-Ingredient Systems
- Small Additions
- Control System

Relative Location to Warehouse

Obviously, the closer the dispensary is to the warehouse the more efficient the material handling considerations can be. There is a lot to be said for the simple use of a pallet jack to bring the raw ingredients, through an air lock, only a few feet to the dispensary.

In reverse, the empty containers only have a few steps to go for disposal. All of this is much more preferable to having to use powered fork lifts or walking stackers in a crowded hallway over a long distance to the dispensary, and then back again with the empties.

Raw Ingredient Containers

Identifying and defining what types of containers that your excipients will be received in will dictate the type of equipment necessary to support their handling and discharge. Paper bags, drums and bulk bags are the typical container types.

Generally, it is desirable to eliminate the handling of bags, if at all possible, and to receive material in lined, fiber drums. This eliminates the need for bag dump stations, the cutting of the bags, the potential for paper and plastic getting into the formulation, as well as the inherent ergonomic disadvantages of having to handle many 50# bags. Handling empty bags is usually dirty and dusty and the trash handling issues are increased.

The use of bulk bags is a very real option, especially with the higher volume excipients. However, there are numerous issues to be considered when handling bulk bags:

- Usually the bulk bags are received on wooden pallets which cannot be brought into the dispensary, so provisions have to be made for transferring the bags onto a GMP acceptable pallet.
- Lifting equipment for bulk bags, that is hygienic, is relatively expensive.
- Equipment stack-up heights can often be prohibitive, in terms of being able to maximize the use of gravity.
- The handling, storing and inventory of partially emptied bulk bags can be challenging.

The common container of choice is a drum (although FIBCs are becoming more and more prevalent). They are modular, stackable, and fairly easy to handle in many ways and lend themselves to gravity discharge as well as simple vacuum transfer, with minimal handling. The empty drums are easily and cleanly handled.

Type of IBC

By definition, a dispensary is used to pre-weigh one or more ingredients into a container or IBC (Intermediate Bulk Container) that will then be transported to the next step in the process for unloading and subsequent refilling and use throughout the process.

Typically, either a drum or a custom IBC, with top fill and bottom discharge is used. The size and shape of this container must be defined early on as the space and the method of filling and discharge will be dependent on this critical decision.

Critical to making this decision is an understanding of the batch sizes and flow characteristics of each of the excipients to be handled in the dispensary. Basic decisions to be made include the following:

- Holding Volume of IBC. Remember that if the IBC is to be blended then it must have about 50% more volume than the actual product volume.
- Type and size of discharge valve, i.e. will you use cone valve technology, split butterfly valve technology or more traditional and less expensive butterfly valves, this all being the subject of another paper.
- How the IBC's will be filled can effect their inlet configuration, overall height and cost.
- Materials of construction, i.e. stainless steel or less expensive polyethylene containers, remembering that poly absorbs odor and stain.

Weighing and Check-weighing

There are two primary considerations when Batch weighing:

1. It is imperative to define the lowest level of acceptable accuracy. This can effect the entire system design and either make or alleviate problems later on.
2. FDA embraces a gain-in-weight weighment of the IBC because it proves that the material is actually in the container, as opposed to loss-in-weight where the scale may register the lost weight but the IBC may not have received it all, if caught up in a chute, flex connection or the like.

What this says is that you should always have, at a minimum, a gain-in-weight scale whether it is being used as the primary batching scale or only a check-weigh scale (or possibly both).

The following primary scaling scenarios should be considered:

Scenario A - Accurate GIW directly into IBC

Feed your ingredients directly into the IBC which is staged on a scale.

- This requires an accurate feed system above the IBC and under whatever the source of powder is, i.e. a drum, a vacuum conveyor or a bulk bag.
- Accuracy is limited by the usually larger gross range of the scale.
- With this approach the source of product will not be emptied so there will be partial containers to deal with.
- If you over charge, you cannot remove the material and the batch will have to be aborted and the IBC emptied.
- There may be cross contamination issues if a single feed system is used.
- Usually the lowest profile system as well as the least expensive.

Scenario B - Accurate GIW Scale Hopper and Dump

Feed your ingredients into a scale hopper on an accurate gain-in-weight basis and then discharge the entire contents directly to the IBC below.

- This scale hopper can be made as small as possible and with as small of a gross range as possible, providing the highest level of accuracy.
- This requires an accurate feed system above the hopper and under whatever the source of powder is, i.e. a drum, a vacuum conveyor or a bulk bag.
- This method is conducive to feeding multiple ingredients into the same hopper. At the same time it is completely dependent upon the complete discharge of all material in it.

Scenario C - Accurate GIW Scale Hopper, Dump, and Checkweigh

This is Scenario B but with a check-weigh scale under the IBC to confirm that all of the material was in fact received by the IBC, within the limits of the scale accuracy.

Scenario D - Accurate LIW Scale Hopper

With this arrangement a scale hopper is filled to some weight greater than the intended batch size and then the batch is produced on a loss-in-weight basis directly to the IBC.

- The hopper can be as small as the largest batch of excipient, usually permitting lower scale range and higher accuracy.
- This approach would be used where the scale hopper is going to be dedicated to a particular excipient as it is filled with slightly more product than the batch size.
- This requires an accurate feeder on the scale hopper discharge.

Scenario E - Accurate LIW Scale Hopper, Checkweigh

This is Scenario D but with a check-weigh scale under the IBC to confirm that all of the material was in fact received by the IBC, within the limits of the scale accuracy.

To Sieve or Not to Sieve

Whether you have to sieve the product or not is a major decision which effects price, stack-up and potentially accuracy. Sieving is considered to either remove lumps of material that have agglomerated in the container and which are not desirable to the process and/or to remove any foreign material such as paper, plastic or foreign items.

This is not a decision that can usually be made by an outside party. Rather it is a quality based decision that must be consistent with the users operating/process experience as well as with the quality of the raw material received.

Batching Feeder

No matter what the scaling system scenario a batch feeder device will be necessary. The feeder needs to be accurate, hygienic and ideally simple. The primary candidates for consideration are usually the following:

Sanitary Rotary Valve – We have found these to be an optimal choice in most circumstances. By means of direct control of the valve vane (which oscillates back and forth over 180°), we can control the flow of product during “bulk” and “dribble” modes and achieve great accuracies. It is pneumatically operated and easily disassembled for cleaning.

Sanitary Pinch Valve – These pneumatically operated bladder-style valves are available up to 3” in diameter and a fluidizing feature may be necessary with some materials. Accuracies of 10 grams, scale permitting, can be achieved and its one piece sanitary bladder makes it simple and hygienic.

Vibratory Feeder - Specially designed to feed product horizontally from a discharge hopper to the receiving container, a vibratory feeder is a simple, safe, and inexpensive choice for getting a controlled feed. The tubular or flat tray and vibratory drive motor can be designed from small to large to accommodate nearly any project specific requirements.

Screw Feeder – screw feeders are often considered but are expensive, complex, hard to clean, and potentially dangerous.

How to Transfer the Excipient

Getting the excipient from its original container and into the scaling system is a major consideration. Gravity and Vacuum Transfer are the two major considerations:

Gravity – gravity is usually best because equipment requirements and cleaning are usually considered to be minimal. However, stackup heights, material handling issues and speed can sometimes minimize the perceived advantages.

Using gravity, means that the ingredients must be brought from the warehouse somewhere "upstairs" to a charging room above the IBC's and all of the trash or empty containers returned. This requires an elevator, potential hall traffic issues, as well as ergonomic, house keeping, and hygiene issues.

Vacuum Transfer – most peoples' immediate reaction to the use of vacuum transfer is "NO". Their minds conjure up pictures of PD blowers, large vessels, many filters, isolation valves, motors and starters and lots of tubing to clean. This is not an accurate picture of vacuum conveying.

Vacuum conveying is a much more attractive option when you realize that it is possible to convey up to 3,000 pounds per hour using only 25 scfm of compressed air (which doesn't see the product), with a vessel that is light, modular, and has washable/disposable filters. Add to that the notion of using disposable hose and the possible benefits of vacuum transfer become clear.

This method of vacuum transfer can permit much lower profile stack-ups, economy compared to drum lifts/ inverters, is completely quiet, has no moving parts, and is very simple to clean. The fact that there are no motors or electrical controls makes its installation very simple and inexpensive. Further, all raw materials can be kept on the lower floor.

As with every other aspect of a dispensary design, there is no one right or best way to accomplish product transfer. The pros and cons, in combination with the other considerations must be weighed and evaluated in the context of the developing design.

Dedicated or Multi-Ingredient Systems

Another major consideration in the design of a dispensary is whether or not to dedicate scale hoppers and transfer equipment to a given excipient. The main, inherent advantage to product dedicated systems is reducing the cleaning efforts and eliminating any chances of cross contamination between ingredients, which may otherwise be a consideration. If these advantages are real then dedicated systems may have to be considered.

If vacuum transfer is used, they usually would be dedicated to a given excipient any way, but could serve a common scale hopper. Alternatively completely dedicated scale hoppers may be considered.

The negative aspects of product dedication are the increased costs and, if dedicated scale hoppers are used, the need to index the IBC from fill station to fill station.

Again, the pros and cons must be evaluated and entered into the equation.

Small Additions

Many formulations call for relatively small quantities of an ingredient to be added to the IBC. These are usually hand weighed into a container, of some sort, which we call a SAC (small add container). Considerations for these small additions include the following:

- How small is small, ie. where do you draw the line between manual weighing and the use of a transfer system? Ergonomics will usually drive this decision.
- Should the material be sieved?
- What kind of container should you use?
- How will the container be moved and its contents transferred to the IBC.
- What level and kind of dust control is required for this manual operation.
- Should the control system incorporate the small additions and be designed to prompt the operator through all steps of the weighment, the label printing and the physical transfer to the IBC.
- Should the small adds be processed right in the main dispensary and be integrated into the bulk excipient handling process, or separated?

The answers to all these questions effect the layout, the IBC design, the controls, the material handling and potentially every aspect of the dispensary design.

Control System

Just as with every other aspect of a dispensary there can be a variation of options in the type of control system to be used.

A dispensary can be designed without the use any PLC's at all, which can be attractive in some ways, but very limiting in others. Simple, proprietary batch controllers such as Mettler Toledo's IND Series Controllers can handle all of the weighing needs, can be programmed to provide a vast number of recipes, as well as a certain level of operator prompting with limited outputs for peripheral control.

If more sophisticated control is desired or necessary the batch controllers should still be used to interface with the scale and provide the built in filters for vibration, stability and all of the other tuning options normally inherent to the controller, not to mention scale calibration.

There is no sense in trying to replicate all of these functions in a PLC when a company like Mettler Toledo has spent millions of dollars developing their controllers tuning capabilities.

If a PLC and an OIT are going to be used additional considerations include the following:

- How much spare I/O should be incorporated? 25% minimum is recommended.
- Is an Ethernet connection needed either now or may it be convenient in the future? It's worth the investment if you anticipate linking to a PC or future SCADA system.
- Monochrome or Color OIT – color is recommended
- Screen size of OIT – bigger is better.
- What hardware and software standards exist and should be utilized, to assure in-plant continuity.
- What level of archiving is required?
- What kind of printer, label and batch summary report format requirements do you have? This can greatly affect the software program and the effort/cost to produce it.
- Should a PC be used in the control system? PC's don't have to be expensive, industrial frame PC's. They can be desktops in an appropriate enclosure and can greatly facilitate the programming efforts and afford more flexibility to the operation of the system.
- A major control consideration is whether or not you need/want to comply with the Electronic record / Electronic Signature regulation Final Rule (FDA 21 CFR Part 11).

In Summary

As we indicated at the outset, designing an excipient dispensary is a process that involves a great deal of collaboration and discussion between all of the interested disciplines.

There is no one right way and every facility has its own set of interests, priorities, space constraints, and personal/personnel preferences.

For this reason, designing the dispensary is a process that must begin by understanding and defining all of these variables so that the designer can incorporate and/or address all of them into the initial conceptual proposal.

IEDCO has quite a bit of experience in this area and would welcome an opportunity to participate in the design process of your dispensary.

We look forward to your invitation.

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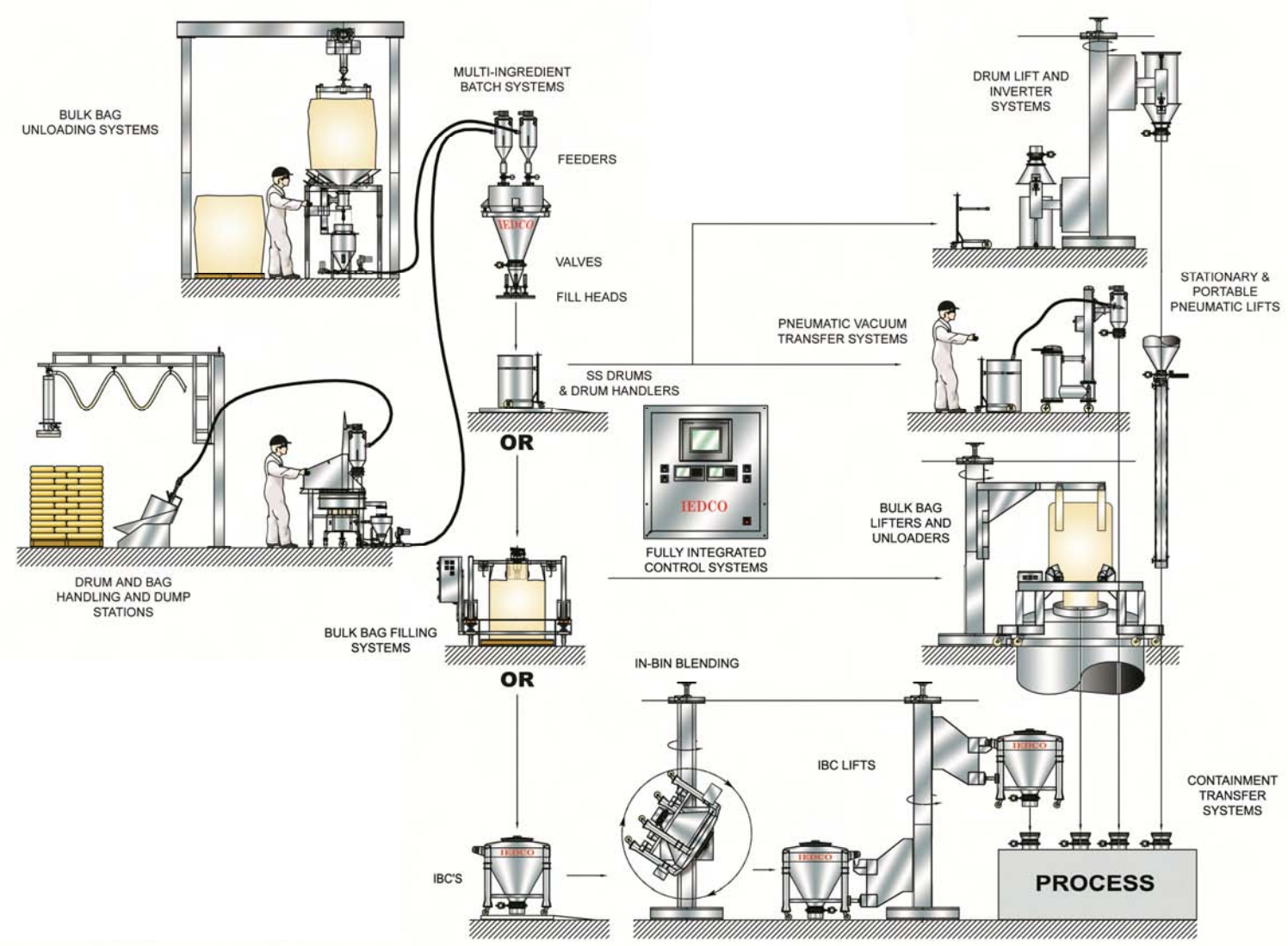

IEDCO is dedicated to the engineering, design, manufacture, and installation of powder and tablet handling systems and technologies.

IEDCO's core business is getting powders and tablets from Point "A" to Point "B" in as reliable, as safe, as contained, and as ergonomically acceptable a way as possible.

We are an innovative engineering company that provides our clients with Single Source Engineered Solutions to their specific powder and/or tablet handling application challenges.

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