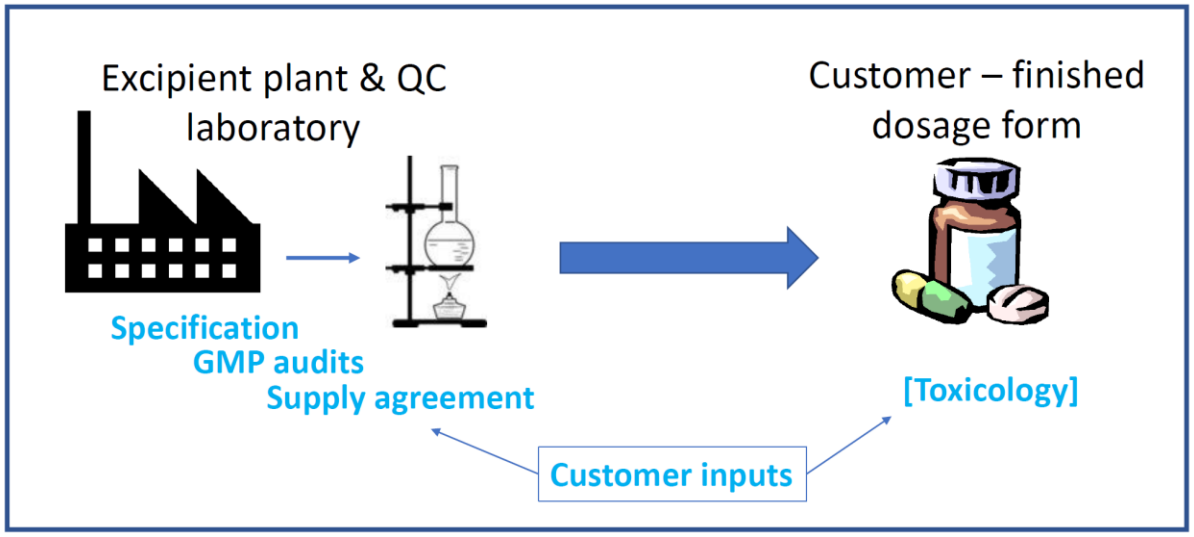
Repurposing Materials for use as Pharmaceutical Excipients

Background

When choosing excipients for use in a medicinal product, the default position is to select ones which have an existing pharmaceutical use. However, there may be situations in which the required functionality can't be achieved by using an established excipient and an ingredient being used exclusively in a non-healthcare sector may have the desired properties. While not necessarily straightforward, repurposing such ingredients for pharmaceutical excipient use is generally feasible and this post highlights some of the issues to consider before embarking on such a project.



Specification

Central to a repurposing exercise is to establish a specification for the material which will define its use as a pharmaceutical excipient.

Depending on its current field of use, the existing specification for a non-pharma ingredient may be rudimentary and/or have broad limits on product attributes. For pharmaceutical excipient use, a robust specification will need to be implemented to ensure that batches reproducibly deliver the required chemical and physical attributes. Tests to meet pharmaceutical regulatory requirements will need to be incorporated where appropriate e.g. organic and inorganic residues, microbiological quality.

The material is undoubtedly being selected for pharmaceutical excipient use because it possesses a unique functionality. That functionality will need to be defined within the material specification and is often the factor which will distinguish pharmaceutical excipient use from existing use. Attributes which define functionality might include degree of chemical substitution, viscosity, molecular weight or particle size distribution.

As part of the specification-setting process, one should also look for related materials (e.g. similar chemical or physical forms) in the major pharmacopoeias (or Food Chemicals Codex if applicable) and assess whether their monographs include any additional tests which are relevant to the new excipient's specification.

Manufacture

A quality audit is required of the manufacturer's plant and QC laboratories to determine the extent of compliance with cGMPs. Ingredients derived from natural products will present extra challenges in terms of controls and ensuring acceptable batch-to-batch variability.

For manufacturers which are not active in the pharmaceutical space, the expected quality requirements (and associated costs) may prove too onerous in relation to the commercial opportunity presented by excipient manufacture (or the cost demands imposed on the customer by the manufacturer, too high).

Toxicology

The existing uses of the material under consideration or uses of chemically related materials will determine the extent to which bespoke toxicology studies will be required to support a future application as a pharmaceutical excipient. Clearly, a material intended for oral administration with an existing food use or for topical administration with an existing cosmetic use will present fewer barriers than a purely industrial chemical which has no current human or animal use by the intended route of administration. Toxicology testing of the excipient can typically be incorporated into the regulatory drug product safety studies.

Unless the new material has an enabling role that cannot be replicated by an established pharma excipient, it's unlikely that the expense, time and risks associated with generating a comprehensive toxicology package will be justified.

Commercial considerations

The commercial challenge is perhaps one of the greatest to repurposing a material for pharmaceutical excipient use. In their non-pharma use we're typically dealing with high volume, low value commodities. Conversely, pharma excipient use will often require relatively low volumes of material. Consequently, an opportunity to repurpose their material for pharmaceutical excipient use may be of little commercial interest to the manufacturer unless value can be added; as suggested earlier, the opportunity will be even less attractive if the customer is demanding significant changes to facilities or procedures to meet their GMP requirements. One way for the manufacturer to add value would be to produce a bespoke "pharma grade" material with an enhanced specification. If there's a significant price premium, sales could be sufficiently attractive even though volumes are low. On the other hand, if the cost premium imposed by the manufacturer is too high, its use as an excipient might not be economically viable.

Equally, unless volumes and/or value are very high, having a second source may not be feasible. Therefore, it's essential to ensure a robust supply agreement is in place to minimise disruptions to future supplies should, for example, the manufacturer intend to change the raw materials, product specifications or even cease manufacture altogether. Good communications between the manufacturer and customer are essential to prevent changes, however minor, being implemented without the customer being made aware.

Final thoughts

If a non-pharma material has been identified as critical to enabling development of a drug product or delivery system, pathways exist for commercialisation. However, comprehensive due diligence is essential to reduce the risk of unanticipated costs, technical obstacles or safety issues, all of which could result in a failure to repurpose the material for excipient use.