Table VII: Effect of particle size on capsule filling.[9]

Median particle size	Properties	Tamp filling machines	Dosator nozzle machines
>150 μm	Excellent flow	Weight uniformity may suffer due to 'splashing' of the blend as the pins descend into the powder bed. Fill wt. may be difficult to achieve as blend lacks compressibility	Generally do not form cohesive plugs – dosator not recommended
100–150 μm	Plug strength may be variable	Increase level of microcrystalline cellulose	
50–100 μm	Ideal plug formation but flow may need improving	Plug formation controlled via tamping force	
20–50 μm	Sticking & poor flow	May be fillable by optimizing levels of lubricant and glidant, or via granulation	
<20 μm	Excessive adhesion to metal parts & very poor flow	Not usually fillable – granulation necessary	

with processing of the formulation or enhance/control the ability of the formulation to deliver the API to the therapeutic site of action. By modifying the physicochemical properties of excipients such as particle size, morphology and surface chemistry (to name but a few) the functionality may be tailored to suit specific applications. Furthermore, APIs that were once considered to be unsuitable for development due to poor solubility and/or bioavailability may now be revisited as candidates. Care should always be taken that the excipients selected are both physically stable and chemically inert in order to ensure the robustness of the formulation and the safety of the patient.

Despite the present wealth of knowledge generated around excipients for oral solid dosage forms, there is still a large amount of research being conducted by both industry and academia. Areas include the development of coprocessed excipients using methods such as spray-drying, or the production of combination excipients, where two different excipients are chemically linked together. These methods may confer the advantages of both excipients within the same product. The role of quality by design (QbD) in the selection of excipients is also expected to become increasingly more prominent with the justification of excipient selection occurring earlier in the development process.

Over the years, awareness of the role of excipients in the performance of dosage forms has increased drawing attention from regulators, for example with the release of guidance around safety evaluations for novel excipients.[57] As globalization continues, it is expected that the number of excipient manufacturers in developing countries will increase. This will result in an increase in the volume of imports from and outsourcing of manufacturing operations to countries with less developed regulatory systems than areas such as the US, EU and Japan. As such it is expected that cGMP guidance from the regulators concerning excipient manufacture and supply will be modernised in order to ensure continued robustness and safety of the ingredients of all medicines.[58]

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