Guidance for Industry SUPAC: Manufacturing Equipment Addendum

DRAFT GUIDANCE

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U.S. Department of Health and Human Services Food and Drug Administration Center for Drug Evaluation and Research (CDER)

> April 2013 CMC

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U.S. Department of Health and Human Services Food and Drug Administration Center for Drug Evaluation and Research (CDER)

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Guidance for Industry¹ **SUPAC: Manufacturing Equipment Addendum**

This draft guidance, when finalized, will represent the Food and Drug Administration's (FDA's) current

thinking on this topic. It does not create or confer any rights for or on any person and does not operate to

bind FDA or the public. You can use an alternative approach if the approach satisfies the requirements of

the applicable statutes and regulations. If you want to discuss an alternative approach, contact the FDA

staff responsible for implementing this guidance. If you cannot identify the appropriate FDA staff, call

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I. INTRODUCTION

the appropriate number listed on the title page of this guidance.

This draft guidance combines and supersedes the following scale-up and post-approval changes (SUPAC) guidances for industry: (1) SUPAC-IR/MR: Immediate Release and Modified Release Solid Oral Dosage Forms, Manufacturing Equipment Addendum, and (2) SUPAC-SS Nonsterile Semisolid Dosage Forms, Manufacturing Equipment Addendum.² It removes the lists of manufacturing equipment that were in both guidances and clarifies the types of processes being referenced.

This draft SUPAC addendum should be used in conjunction with the following SUPAC guidances for industry:³ (1) Immediate Release Solid Oral Dosage Forms — Scale-Up and Post-Approval Changes: Chemistry, Manufacturing and Controls, In Vitro Dissolution Testing, and In Vivo Bioequivalence Documentation, (2) SUPAC-MR: Modified Release Solid Oral Dosage Forms Scale-Up and Post-Approval Changes: Chemistry, Manufacturing and Controls; In Vitro Dissolution Testing and In Vivo Bioequivalence Documentation, and (3) SUPAC-SS: Nonsterile Semisolid Dosage Forms, Scale-Up and Post Approval Changes: Chemistry Manufacturing and Controls; In Vitro Release Testing and In Vivo Bioequivalence Documentation.⁴

The SUPAC guidances define: (1) levels of chemistry, manufacturing, and control change; (2) recommended chemistry, manufacturing, and controls tests for each level of change; (3) recommended in vitro dissolution and release tests and/or in vivo bioequivalence tests for each level of change; and (4) recommended documentation that should support the change for new drug applications and abbreviated new drug applications.

¹ This guidance has been prepared by the Office of Pharmaceutical Science in the Center for Drug Evaluation and Research (CDER) at the Food and Drug Administration.

² For this guidance only, the new document that is a combination of these two guidances will be referred to as the SUPAC addendum.

³ We update guidances periodically. To make sure you have the most recent version of a guidance, check the FDA Drugs guidance Web page at

http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm.

⁴ For this guidance only, this collective group of guidances will be referred to as SUPAC guidances.

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This draft SUPAC addendum, together with the SUPAC guidances, is intended to help you, the manufacturer, determine the documentation you should submit to FDA regarding manufacturing equipment changes.

FDA's guidance documents, including this guidance, do not establish legally enforceable responsibilities. Instead, guidances describe the Agency's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word *should* in Agency guidances means that something is suggested or recommended, but not required.

II. BACKGROUND

When the SUPAC equipment addenda were published with tables referencing specific equipment, the tables were misinterpreted as equipment required by FDA. FDA recognizes that scientific innovation and technology advancement are commonplace and play a significant role in pharmaceutical development, manufacturing, and quality assurance, and we are concerned that such a misunderstanding could discourage advancements in manufacturing technologies. Therefore, this revised draft SUPAC addendum contains general information on SUPAC equipment and no longer includes tables referencing specific equipment. This draft guidance also includes changes to clarify the types of processes being referenced.

III. DISCUSSION

 The information in this draft guidance is presented in broad categories of unit operation. For immediate or modified release solid oral dosage forms, broad categories include blending and mixing, drying, particle size reduction/separation, granulation, unit dosage, coating and printing, and soft gelatin capsule encapsulation. For nonsterile semisolid dosage forms, broad categories include particle size reduction and/or separation, mixing, emulsification, deaeration, transfer, and packaging. Definitions and classifications are provided. For each operation, equipment is categorized by class (operating principle) and subclass (design characteristic). Examples of types of equipment, but not specific brand information, are given within the subclasses.

 When assessing manufacturing equipment changes from one class to another or from one subclass to another, you can follow a risk-based approach that includes a rationale and complies with the regulations, including the CGMP regulations.^{5, 6} We also recommend addressing the impact on the product quality attributes of equipment variations (via process parameters) when designing and developing the manufacturing process.

When making equipment changes, you will need to determine the filing requirement.⁷ The SUPAC guidances provide information on how to do so. FDA will assess the changes based on the types of equipment changes being considered. If you choose an approach that exceeds the SUPAC guidances and addendum, FDA will assess the changes provided they are supported by a suitable risk-based assessment.

⁵ 21 CFR 314.70.

⁶ 21 CFR 210-211.

⁷ 21 CFR 314.70.

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used to	time of the equipment change, you should have available the scientific data and rationale of determine the type of change and documentation required. This information is subject to eview at its discretion.		
IV.	SUPAC IR/MR INFORMATION		
A.	Particle Size Reduction/Separation		
1.	Definitions		
	a. Unit Operations		
	 Particle Size Reduction: The mechanical process of breaking particles into smaller pieces via one or more particle size reduction mechanisms. The mechanical process used generally is referred to as milling. 		
	 Particle – Refers to either a discrete particle or a grouping of particles, generally know as an agglomerate. 		
	b. Particle Size Reduction Mechanisms		
	 Impact - Particle size reduction by applying an instantaneous force perpendicular to the particle/agglomerate surface. The force can result from particle-to-particle or particle-to-mill surface collision. 		
	 Attrition - Particle size reduction by applying a force in a direction parallel to the particle surface. 		
	• Compression - Particle size reduction by applying a force slowly (as compared to Impact) to the particle surface in a direction toward the center of the particle.		
	 Cutting - Particle size reduction by applying a shearing force to a material. 		
	ii. Particle Separation: Particle size classification according to particle size alone.		
	b. Operating Principles		
	i. Fluid Energy Milling		
	Particles are reduced in size as a result of high-speed particle-to-particle impact and/or attrition; also known as micronizing.		

ii. Impact Milling

130		
131		Particles are reduced in size by high-speed mechanical impact or impact
132		with other particles; also known as milling, pulverizing, or comminuting.
133		
134	iii.	Cutting
135		
136		Particles are reduced in size by mechanical shearing.
137		
138	iv.	Compression Milling
139		
140		Particles are reduced in sized by compression stress and shear
141		between two surfaces.
142		
143	v.	Screening
144		
145		Particles are reduced in size by mechanically induced attrition through a
146		screen. This process commonly is referred to as milling or
147		deagglomeration.
148		T 11 M'II'
149	V1.	Tumble Milling
150		Destining our moderned in size has attrition atilizing eminding modic
151		Particles are reduced in size by attrition utilizing grinding media.
152 153	x/ii	Separating
153	vii.	Separating
155		Particles are segregated based upon particle size alone and without any
156		significant particle size reduction. This process commonly is referred to as
157		screening or bolting.
158		screening or boiting.
159	2. Equipment C	lassifications
160	2. Equipment et	assifications
161	a. Fluid	Energy Mills
162		
163	Fluid	energy mill subclasses have no moving parts and primarily are distinguished
164		one another by the configuration and/or shape of their chambers, nozzles,
165		assifiers.
166		
167	• Ta	ingential Jet
168		pop/Oval
169		pposed Jet
170	•	oposed Jet with Dynamic Classifier
171		uidized Bed
172		xed Target
173		oving Target
173		gh Pressure Homogenizer
174	▼ П	gn i ressure montogenizer
113		

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176	b. Impact Mills
177	
178	Impact mill subclasses primarily are distinguished from one another by the
179	configuration of the grinding heads, chamber grinding liners (if any), and
180	classifiers.
181	
182	Hammer Air Swept
183	Hammer Conventional
184	• Pin/Disc
185	• Cage
186	
187	c. Cutting Mills
188	
189	Although cutting mills may differ from one another in whether the knives are
190	movable or fixed and in the classifier configuration, no cutting mill subclasses
191	have been identified.
192	
193	d. Compression Mills
194	
195	Although compression mills may differ from one another in whether one or both
196	surfaces are moving, no compression mill subclasses have been identified.
197	
198	e. Screening Mills
199	
200	Screening mill subclasses primarily are distinguished from one another by the
201	rotating element.
202	
203	Rotating Impeller
204	Rotating Screen
205	Oscillating Bar
206	
207	f. Tumbling Mills
208	
209	Tumbling mill subclasses primarily are distinguished from one another by the
210	grinding media used and by whether the mill is vibrated.
211	
212	Ball Media
213	Rod Media
214	Vibrating
215	· Violating
216	g. Separators
217	g. Separators
218	Separator subclasses primarily are distinguished from one another by the
219	mechanical means used to induce particle movement.
220	meetament means assu to made particle movement.
221	Vibratory/Shaker
222	• Centrifugal
<i>LLL</i>	• Cenunugai

223				
224		B.	Blending and	l Mixing
225				
226	1.	Defini	tions	
227		v		
228		a.	Unit Operatio	ns
229			1	
230			Blending and	Mixing: The reorientation of particles relative to one another in
231			_	ve uniformity.
232				
233		h.	Operating Pri	nciples
234		•	operating rate	
235			i.	Diffusion Blending (Tumble)
236				2 interior 2 ionomy (1 amort)
237				Particles are reoriented in relation to one another when they are
238				placed in random motion and interparticular friction is reduced
239				as the result of bed expansion (usually within a rotating
240				container); also known as tumble blending.
241				container), also known as turnore orenang.
242			ii.	Convection Mixing
243			11.	Convection whalig
244				Particles are reoriented in relation to one another as a result
245				of mechanical movement; also known as paddle or plow
245				mixing.
247				mixing.
248			iii.	Pneumatic Mixing
			111.	Flieumatic Wixing
249250				Particles are reoriented in relation to one another as a result of
251				the expansion of a powder bed by gas.
252	2	Earling	mant Classifias	
253	2.	Equipi	nent Classifica	titons
254			Diffusion Mix	rans (Tymhla)
255		a.	Diffusion Mix	ers (Tumble)
256			D:cc:	
257				er subclasses primarily are distinguished by geometric shape and
258			the positionin	g of the axis of rotation.
259				
260			 V-blender 	
261				one Blenders
262			• Slant Con-	e Blenders
263			• Cube Bler	nders
264			• Bin Blend	ers
265			• Horizonta	l/Vertical/Drum Blenders
266			Static Cor	ntinuous Blenders
267				Continuous Blenders
268			_ j	
269		b.	Convection M	lixers

				Draji — Noi joi impiementation
270				
271			Convection bl	ender subclasses primarily are distinguished by vessel shape and
272			impeller geom	
273			1 &	
274			Ribbon Bl	enders
275				Screw Blenders
276			 Planetary 	
277			 Forberg B 	
278				l Double Arm Blenders
279				
				High Intensity Mixers
280				ligh Intensity Mixers
281			• Diffusion	Mixers (Tumble) with Intensifier/Agitator
282 283			Pneumatic Mi	Y o w o
284		c.	Fileumatic IVII	Xels
285			Although pne	umatic mixers may differ from one another in vessel geometry, air
286				nd air nozzle configuration, no pneumatic mixer subclasses have
287			been identifie	
288			occii identific	u.
289				
290		C.	Granulation	
291		C.	Granulation	
292	1.	Defini	itions	
293		_ 5,		
294		a.	Unit Operatio	ns
295			•	
296			Granulation:	The process of creating granules. The powder morphology is
297			modified thro	ugh the use of either a liquid that causes particles to bind through
298			capillary force	es or dry compaction forces. The process will result in one or more
299			of the following	ng powder properties: enhanced flow; increased compressibility;
300			densification;	alteration of physical appearance to more spherical, uniform, or
301			larger particle	s; and/or enhanced hydrophilic surface properties.
302				
303		b.	Operating Prin	nciples
304				
305			i.	Dry Granulation
306				
307				Dry powder densification and/or agglomeration by direct
308				physical compaction.
309				
310			ii.	Wet High-Shear Granulation
311				
312				Powder densification and/or agglomeration by the incorporation
313				of a granulation fluid into the powder with high-power-per-unit
314				mass, through rotating high-shear forces.
315				

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iii.	Wet Low-Shear Granulation

Powder densification and/or agglomeration by the incorporation of a granulation fluid into the powder with low-power-per-unit mass, through rotating low-shear forces.

iv. Low-Shear Tumble Granulation

Powder densification and/or agglomeration by the incorporation of a granulation fluid into the powder with low-power-per-unit mass, through rotation of the container vessel and/or intensifier bar.

Extrusion Granulation v.

Plasticization of solids or wetted mass of solids and granulation fluid with linear shear through a sized orifice using a pressure gradient.

vi. **Rotary Granulation**

Spheronization, agglomeration, and/or densification of a wetted or non-wetted powder or extruded material. This is accomplished by centrifugal or rotational forces from a central rotating disk, rotating walls, or both. The process may include the incorporation and/or drying of a granulation fluid.

Fluid Bed Granulation vii.

Powder densification and/or agglomeration with little or no shear by direct granulation fluid atomization and impingement on solids, while suspended by a controlled gas stream, with simultaneous drying.

Spray Dry Granulation viii.

A pumpable granulating liquid containing solids (in solution or suspension) is atomized in a drying chamber and rapidly dried by a controlled gas stream, producing a dry powder.

ix. Hot-melt Granulation

An agglomeration process that utilizes a molten liquid as a binder(s) or granulation matrix in which the active pharmaceutical ingredient (API) is mixed and then cooled down followed by milling into powder. This is usually accomplished in a temperature controlled jacketed high shear granulating tank

359 360

363		or using a heated nozzle that sprays the molten binders(s) onto
364		the fluidizing bed of the API and other inactive ingredients.
365		
366	2.	Equipment Classification
367		
368		a. Dry Granulator
369		
370		Dry granulator subclasses primarily are distinguished by the densification force
371		application mechanism.
372		
373		• Slugging
374 37 <i>5</i>		Roller Compaction
375		1 Wat High Chang Convolution
376 377		b. Wet High-Shear Granulator
378		Wet high-shear granulator subclasses primarily are distinguished by the
378 379		geometric positioning of the primary impellers; impellers can be top, bottom,
380		or side driven.
381		of side differi.
382		 Vertical (Top or Bottom Driven)
383		Horizontal (Side Driven)
384		• Horizontai (Side Driven)
385		c. Wet Low-Shear Granulator
386		c. Wet Low Shear Grandiator
387		Wet low-shear granulator subclasses primarily are distinguished by the
388		geometry and design of the shear inducing components; shear can be induced
389		by rotating impeller, reciprocal kneading action, or convection screw action.
390		by folding impener, reciprocal kneading action, or convection serew action.
391		Planetary
392		Kneading
393		• Screw
394		- Belew
395		d. Low-Shear Tumble Granulator
396		di 2011 piloti Tamore Granarator
397		Although low-shear tumble granulators may differ from one another in vessel
398		geometry and type of dispersion or intensifier bar, no low-shear tumble
399		granulator subclasses have been identified.
400		
401		• Slant cone
402		 Double cone
403		• V-blender
404		
405		e. Extrusion Granulator
406		

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407		Extrusion granulator subclasses primarily are distinguished by the
408		orientation of extrusion surfaces and driving pressure production
409		mechanism.
410		
411		Radial or Basket
412		 Axial
413		• Ram
414		Roller, Gear, or Pelletizer
415		
416	f.	Rotary Granulator
417		·
418		Rotary granulator subclasses primarily are distinguished by their structural
419		architecture. They have either open top architecture, such as a vertical centrifugal
420		spheronizer, or closed top architecture, such as a closed top fluid bed dryer.
421		
422		• Open
423		• Closed
424		
425	g.	. Fluid Bed Granulator
426	S	
427		Although fluid bed granulators may differ from one another in geometry,
428		operating pressures, and other conditions, no fluid bed granulator subclasses
429		have been identified.
430		
431	h.	Spray Dry Granulator
432		
433		Although spray dry granulators may differ from one another in geometry,
434		operating pressures, and other conditions, no spray dry granulator subclasses have
435		been identified.
436		
437	i.	Hot-melt Granulator
438	1.	That ment offundation
439		Although, hot-melt granulator may differ from one another in primarily melting the
440		inactive ingredient (particularly the binder or other polymeric matrices), no
441		subclasses have been indentified yet.
		subclasses have been indentified yet.
442	NT /	
443	Note:	
444	0 1	iece of equipment is capable of performing multiple discrete unit operations (mixing,
445 446		drying), the unit was evaluated solely for its ability to granulate. If multifunctional ncapable of discrete steps (fluid bed granulator/drier), the unit was evaluated as an
446	integrated u	
448	micgrateu u	III.
449	D.	Drying
450	υ.	~~J.~~ g
451	1. Defin	itions
TJ 1	ւ. Dejin	III III

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453	a. Unit Operation	ı
454		
455	Drying: The re	emoval of a liquid from a solid by evaporation.
456		
457	b. Operating Prin	ciples
458		
459	i.	Direct Heating, Static Solids Bed
460		
461		Heat transfer is accomplished by direct contact between the wet
462		solids and hot gases. The vaporized liquid is carried away by the
463		drying gases. There is no relative motion among solid particles.
464		The solids bed exists as a dense bed, with the particles resting upon
465		one another.
466		
467	ii.	Direct Heating, Moving Solids Bed
468		
469		Heat transfer is accomplished by direct contact between the wet
470		solids and hot gases. The vaporized liquid is carried away by the
471		drying gases. Solids motion is achieved by either mechanical
472		agitation or gravity force, which slightly expands the bed enough to
473		flow one particle over another.
474		
475	iii.	Direct Heating, Fluidized Solids Bed
476		
477		Heat transfer is accomplished by direct contact between the wet
478		solids and hot gases. The vaporized liquid is carried away by the
479		drying gases. The solids are in an expanded condition, with the
480		particles supported by drag forces caused by the gas phase. The
481		solids and gases intermix and behave like a boiling liquid. This
482		process commonly is referred to as fluid bed drying.
483		
484	iv.	Direct Heating, Dilute Solids Bed, Spray Drying
485		
486		Heat transfer is accomplished by direct contact between a highly
487		dispersed liquid and hot gases. The feed liquid may be a solution,
488		slurry, emulsion, gel or paste, provided it is pumpable and capable
489		of being atomized. The fluid is dispersed as fine droplets into a
490		moving stream of hot gases, where they evaporate rapidly before
491		reaching the wall of the drying chamber. The vaporized liquid is
492		carried away by the drying gases. The solids are fully expanded
493		and so widely separated that they exert essentially no influence on
494		one another.
495		
496	v.	Direct Heating, Dilute Solids Bed, Flash Drying

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		v <u> </u>
498		Heat transfer is accomplished by direct contact between wet solids
499		and hot gases. The solid mass is suspended in a finely divided state
500		in a high-velocity and high-temperature gas stream. The vaporized
501		liquid is carried away by the drying gases.
502		
503	vi.	Indirect Conduction, Moving Solids Bed
504		
505		Heat transfer to the wet solid is through a retaining wall. The
506		vaporized liquid is removed independently from the heating
507		medium. Solids motion is achieved by either mechanical agitation
508		or gravity force, which slightly expands the bed enough to flow one
509		particle over another.
510		
511	vii.	Indirect Conduction, Static Solids Bed
512		,
513		Heat transfer to the wet solid is through a retaining wall. The
514		vaporized liquid is removed independently from the heating
515		medium. There is no relative motion among solid particles. The
516		solids bed exists as a dense bed, with the particles resting upon one
517		another.
518		
519	viii	. Indirect Conduction, Lyophilization
520	V 111	maneet conduction, 2) opinization
521		Drying in which the water vapor sublimes from the product after
522		freezing.
523		necznig.
524	ix.	Gas Strinning
	IA.	Gas Stripping
525		
526		Heat transfer is a combination of direct and indirect heating. The
527		solids motion is achieved by agitation and the bed is partially
528		fluidized.
529		
530	Х.	Indirect Radiant, Moving Solids Bed
531		
532		Heat transfer is accomplished with varying wavelengths of energy.
533		Vaporized liquid is removed independently from the solids bed.
534		The solids motion is achieved by mechanical agitation, which
535		slightly expands the bed enough to flow one particle over one
536		another. This process commonly is referred to as microwave
537		drying.
538		
539	2. Equipment Classif	ications
540	_	
541	 a. Direct Hear 	ting, Static Solids Bed

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543	Static solids bed subclasses primarily are distinguished by the method of
544	moving the solids into the dryer.
545	·
546	Tray and Truck
547	• Belt
548	
549	b. Direct Heating, Moving Solids Bed
550	
551	Moving solids bed subclasses primarily are distinguished by the method or
552	technology for moving the solids bed.
553	commerces, for me and some com-
554	Rotating Tray
555	Horizontal Vibrating Conveyor
556	Tionzonal Violating Conveyor
557	c. Direct Heating, Fluidized Solids Bed (Fluid Bed Dryer)
558	c. Direct Heating, Fluidized Solids Bed (Fluid Bed Dryer)
559	Although fluid bed dryers may differ from one another in geometry, operating
560	pressures, and other conditions, no fluidized solids bed dryer subclasses have
561	been identified.
562	been identified.
563	d. Direct Heating, Dilute Solids Bed, Spray Dryer
	d. Direct Heating, Dilute Solids Bed, Spray Dryer
564 565	Although spray dryers may differ from one another in geometry, operating
566	
	pressures, and other conditions, no spray dryer subclasses have been identified
567	a Direct Heating Dilute Solide Ded Flesh Dryon
568	e. Direct Heating, Dilute Solids Bed, Flash Dryer
569 570	Although flock drivers may differ from one enother in geometry, energting
570 571	Although flash dryers may differ from one another in geometry, operating
571	pressures, and other conditions, no flash dryer subclasses have been identified.
572 573	f Indirect Conduction Heating Maying Solids Dad
	f. Indirect Conduction Heating, Moving Solids Bed
574 575	Maxima calida had subalassas mimanily and distinguished by the mathod on
	Moving solids bed subclasses primarily are distinguished by the method or
576 577	technology for moving the solids bed.
577	ם און
578	• Paddle
579	• Rotary (Tumble)
580	 Agitation
581	
582	g. Indirect Conduction Heating, Static Solids Beds
583	
584	No indirect heating, static solids bed shelf dryer subclasses have been
585	identified.
586	
587	h. Indirect Conduction, Lyophilization

589		No lyophilize	r subclasses have been identified.
590	•	G G: :	
591	i.	Gas Stripping	
592			
593			stripping dryers may differ from one another in geometry, shape of
594		•	how fluidizing gas is moved through the bed, no gas stripping dryer
595		subclasses ha	ve been identified.
596			
597	j.	Indirect Radi	ant Heating, Moving Solids Bed (Microwave Dryer)
598			
599		Although mic	crowave dryers may differ from one another in vessel
600		geometry and	the way microwaves are directed into the solids, no
601		indirect radia	nt heating, moving solids bed dryer subclasses have been
602		identified.	
603			
604	Note: If a si	ngle piece of e	quipment is capable of performing multiple discrete unit operations
605			g), the unit was evaluated solely for its ability to dry. The drying
606	equipment w	as sorted into s	similar classes of equipment, based upon the method of heat transfer
607	and the dyna	mics of the sol	ids bed.
608	•		
609	E.	Unit Dosing	
610			
611	1. Defini	tions	
612	J		
613	a.	Unit Operation	on
614		1	
615		Unit Dosing:	The division of a powder blend into uniform single portions for
616		delivery to pa	-
617		r-y p	
618	b.	Operating Pri	nciples
619		operming in	
620		i.	Tabletting
621			Theretains
622			The division of a powder blend in which compression force is
623			applied to form a single unit dose.
624			applied to form a single with dose.
625		ii.	Encapsulating
626			Zneupsuluing
627			The division of material into a hard gelatin capsule. Encapsulators
628			should all have the following operating principles in common:
629			rectification (orientation of the hard gelatin capsules), separation of
630			capsule caps from bodies, dosing of fill material/formulation,
631			rejoining of caps and bodies, and ejection of filled capsules.
632			rejoining of caps and bodies, and ejection of fined capsules.
633		iii.	Dowder Filling
		111.	Powder Filling
634			The division of a nevertain hland into a container also are services
635			The division of a powder blend into a container closure system.

636	2.	Equip	ment Classifications
637		1 1	·
638		a.	Tablet Press
639			
640			Tablet press subclasses primarily are distinguished from one another by the
641			method that the powder blend is delivered to the die cavity. Tablet presses can
642			deliver powders without mechanical assistance (gravity), with mechanical
643			assistance (power assisted), by rotational forces (centrifugal), and in two different
644			locations where a tablet core is formed and subsequently an outer layer of coating
645			material is applied (compression coating).
646			
647			• Gravity
648			Power Assisted
649			• Centrifugal
650			Compression Coating
651			
652			Tablet press subclasses are also distinguished from one another for some special
653			types of tablets where more than one hopper and precise powder feeding
654			mechanism might be necessary.
655			·
656			Micro/ mini tablet press
657			Multi-layer tablet press (bi-layer, tri-layer)
658			
659		b.	Encapsulator
660			
661			Encapsulator subclasses primarily are distinguished from one another by the
662			method that is used for introducing material into the capsule. Encapsulators
663			can deliver materials with a rotating auger, vacuum, vibration of perforated
664			plate, tamping into a bored disk (dosing disk), or cylindrical tubes fitted with
665			pistons (dosator).
666			
667			• Auger
668			• Vacuum
669			 Vibratory
670			 Dosing Disk
671			 Dosator
672			
673		c.	Powder Filler
674			
675			Subclasses of powder fillers primarily are distinguished by the method used to
676			deliver the predetermined amount for container fill.
677			
678			• Vacuum
679			• Auger
680			

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681		F.	Soft (Gelatin (Capsule
682					
683	1.	Defini	itions		
684					
685		a.	Unit (Operation	ns
686					
687				i.	Gel Mass Preparation: The manufacture of a homogeneous,
688					degassed liquid mass (solution) of gelatin, plasticizer, water, and
689					other additives, either in solution or suspension, such as colorants,
690					pigments, flavors, preservatives, etc., that comprise a unique
691					functional gel shell formation. The operation may be performed in
692					discreet steps or by continuous processing. Minor components can
693					be added after the liquid gel mass is made.
694 695				ii.	Fill Miving. The miving of either liquids or solids with other liquids
696				11.	Fill Mixing: The mixing of either liquids or solids with other liquids to form a solution; blending of limited solubility solid(s) with a
697					liquid carrier and suspending agents used to stabilize the blend to
698					form a suspension; or the uniform combination of dry inert and drug
699					active substances to form a dry powder fill suitable for
700					encapsulation. The reader should refer to the other sections of this
701					document for dry fill manufacture.
702					
703				iii.	Encapsulation: The continuous casting of gel ribbons, with liquid
704					fill material being injected between the gel ribbons using a positive
705					displacement pump or, for dry materials being gravity or force fed
706					with capsule formation using a rotary die.
707					
708				iv.	Washing: The continuous removal of a lubricant material from the
709					outside of the formed capsule. The washing operation is unique to
710					each manufacturer's operation and generally uses in-house
711					fabricated equipment. This equipment will not be discussed in this
712					guidance document.
713					
714				v.	Drying: The removal of the majority of water from the capsule's
715					gel shell by tumbling and subsequent tray drying using conditioned
716					air, which enhances the size, shape, and shell physical properties of
717 718					the final product. The drying operation is unique to each
718 719					manufacturer's operation and generally uses in-house fabricated equipment. This equipment will not be discussed in this guidance
720					document.
720					document.
722				vi.	Inspection/Sorting: The process wherein undesirable capsules are
723				***	removed, including misshapen, leaking, and unfilled capsules as
724					well as agglomerates of capsules.
725					
726				vii.	Printing: The marking of a capsule surface for the purpose of
727					product identification, using a suitable printing media or method.

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728					
729	b).	Operati	ing Prir	nciples
730					
731				i.	Mixing
732					
733					The combination of solid and liquid components, including
734					suspending aid(s) at either ambient or elevated temperatures to
735					form a solution, suspension, or dry powder blend for the
736					manufacture of gel mass or fill material. Mixing also includes
737					the incorporation of minor components into the liquid gel mass.
738					
739				ii.	Deaggregation
740					
741					The removal of aggregates using a suitable homogenizer/mill to
742					provide a pumpable fill material. The procedure has minimal
743					effect on the particle size distribution of the initial solid
744					component(s), and is viewed as a processing aid. ⁸
745					1 0
746				iii.	Deaeration
747					
748					The removal of entrapped air from either the gel mass or fill
749					material, solution or suspension. This process can take place in
750					either the mixing vessel, through the application of vacuum, or
751					a separate off-line step.
752					•
753				iv.	Holding
754					
755					The storage of liquid gel mass or fill material in a vessel, with
756					a mixer or without, prior to encapsulation, which also may be
757					equipped with a jacket for either heating or cooling.
758					
759				v.	Encapsulation
760					0
761					The formation of capsules using a rotary die machine. ⁹
762					
763				vi.	Inspection/Sorting
764					
765					The physical removal of misshapen, leaking, or
766					agglomerated capsules, using either a manual or automatic
767					operation.

⁸ Carstensen, J. T., "Theory of Pharmaceutical Systems, Volume 11 Heterogeneous Systems," *Academic Press*, New York, NY, 1973, p 51.

⁹ Lachman, L., Ĥ. A. Lieberman, and J. L. Kanig (Eds.), *The Theory and Practice of Industrial Pharmacy*, Chapter 3, p. 359 (Stanley, J. P.), Philadelphia Lea & Febiger, 1971; Tyle, P. (Ed.), *Specialized Drug Delivery Systems, Manufacturing and Production Technology*, Chapter 10, p. 409 (Wilkinson, P.K. and F.S. Hom), New York; M. Dekker, 1990; Porter, S., *Remington's Pharmaceutical Sciences*, Edition 18, Chapter 89, pp. 1662 - 1665, Easton, Penn.: Mack Publishing Co.

				· · · · · · · · · · · · · · · · · · ·
768			••	D : 4:
769			vii.	Printing
770				
771				The user of this document is asked to refer to the coating/printing
772				section, in which the use of various pieces of equipment are defined
773				and categorized.
774				
775	2.	Equip	ment Classifica	ations
776				
777		a.	Mixers and M	lixing Vessels
778				
779			Mixer and mi	xing vessel subclasses primarily are distinguished by the mixing
780			energy, mixer	type, and whether a jacketed vessel with vacuum capabilities is
781			used in conju	nction with a specific mixer.
782				
783			 Low Ener 	gy Mixer
784			High Ener	
785			• Planetary	
786			•	Vessel With and Without Vacuum
787			• Convention	
788			Convenie	
789		b.	Deaggregator	S
790		0.	Deuggregutor	
791			Deaggregator	subclasses primarily are distinguished by the type of
792				etion imparted to the material.
793			meenamear ac	mon imparted to the material.
794			Rotor/Sta	tor
795			• Roller	
796			Cutting M	fille
797			Stone Mil	
798			 Tumbling 	MIIIS
799			D	
800		c.	Deaerators	
801			D 4 1	
802				classes primarily are distinguished by the air removal path, either
803			•	ulk or through a thin film, and whether it is a batch or in-line
804			process.	
805				
806			 Vacuum V 	
807			 Off Line/I 	n Line
808				
809		d.	Holding Vess	els
810				
811			_	ding vessels may differ from one another, based upon whether they
812			•	with and without integrated mixing capabilities, no holding vessel
813			subclasses hav	ve been identified.

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814					
815			 Jacketed 	vessel w	vith and without mixing system
816					Ç Ç
817		e.	Encapsulator	S	
818			•		
819			Encapsulator	subclass	ses primarily are distinguished by the method used to inject
820			the fill materi	al.	
821					
822			• Positive I	Displace	ment Pump
823			• Gravity o	r Force	Fed
824			•		
825		f.	Inspection/So	orting	
826			-		
827			Inspection/so	rting equ	uipment subclasses primarily are distinguished by the
828			method used	to prese	nt the capsule for viewing and mechanical method of
829			separation.		
830					
831			• Belt		
832			 Vibratory 	7	
833			 Roller 		
834			• Rotary Ta	able	
835			• Electrome	echanica	ા
836					
837		G.	Coating/Prin	nting/D	rilling
838					
839	1.	Definit	tions		
840					
841		a.	Unit Operation	on	
842					
843			i.		ng: The uniform deposition of a layer of material on
844				or aro	und a solid dosage form, or component thereof, to:
845					
846				a.	Protect the drug from its surrounding environment
847					(air, moisture, and light), with a view to improving
848				1	stability.
849				b.	Mask unpleasant taste, odor, or color of the drug.
850				C.	Increase the ease of ingesting the product for the patient.
851				d.	Impart a characteristic appearance to the tablets, which
852					facilitates product identification and aids patient
853					compliance.
854 855				e.	Provide physical protection to facilitate handling. This includes minimizing dust generation in subsequent unit
856					includes minimizing dust generation in subsequent unit operations.
857				f.	Reduce the risk of interaction between incompatible
858				1.	components. This would be achieved by coating one or
859					more of the offending ingredients.

		<i>y y y</i>
860 861		g. Modify the release of drug from the dosage form. This includes delaying, extending, and sustaining drug substance
862		release.
863 864		The coating material deposition typically is accomplished
865		through one of five major techniques:
866		unough one of five major teeninques.
867		a. Sugar Coating - Deposition of coating material onto
868		the substrate from aqueous solution/suspension of
869		coatings, based predominately upon sucrose as a raw
870		material.
871		b. Film Coating - The deposition of polymeric film onto
872		the solid dosage form.
873		c. Core Enrobing - The gelatin coating of gravity or force
874		fed pre- formed tablets or caplets.
875		d. Microencapsulation - The deposition of a coating material
876		onto a particle, pellet, granule, or bead core. The
877		substrate in this application ranges in size from submicron
878		to several millimeters. It is this size range that
879		differentiates it from the standard coating described in 1
880		and 2 above.
881		e. Compression Coating (This topic is addressed in the Unit
882		Dosing section.)
883		
884	ii.	Printing: The marking of a capsule or tablet surface for the
885		purpose of product identification. Printing may be accomplished
886		by either the application of a contrasting colored polymer (ink)
887		onto the surface of a capsule or tablet, or by the use of laser
888		etching.
889		
890		The method of application, provided the ink formulation is not
891		altered, is of no consequence to the physical-chemical properties of
892		the product.
893		
894	iii.	Drilling: The drilling or ablating of a hole or holes through the
895		polymeric film coating shell on the surfaces of a solid oral dosage
896		form using a laser. The polymeric film shell is not soluble in
897		vivo. The hole or holes allow for the modified release of the drug
898		from the core of the dosage form.
899	1 O " D"	. 1
900	b. Operating Prin	nciples
901	:	Pan Coating
902	i.	Pan Coating
903		The uniform deposition of coating material onto the surface of a
904		solid dosage form, or component thereof, while being translated via
905		a rotating vessel.

906		
907	ii.	Gas Suspension
908		
909		The application of a coating material onto a solid dosage form, or
910		component thereof, while being entrained in a process gas stream.
911		
912		Alternatively, this may be accomplished simultaneously by
913		spraying the coating material and substrate into a process gas
914		stream.
915		
916	iii.	Vacuum Film Coating
917		
918		This technique uses a jacketed pan equipped with a baffle system.
919		Tablets are placed into the sealed pan, an inert gas (i.e., nitrogen)
920		is used to displace the air and then a vacuum is drawn.
921		
922	iv.	Dip Coating
923		
924		Coating is applied to the substrate by dipping it into the
925		coating material. Drying is accomplished using pan coating
926		equipment.
927		
928	v.	Electrostatic Coating
929		
930		A strong electrostatic charge is applied to the surface of the
931		substrate. The coating material containing oppositely charged ionic
932		species is sprayed onto the substrate.
933		
934	vi.	Compression Coating
935		
936		Refer to the Unit Dosing section of this document.
937	vii.	Ink-Based Printing
731	VII.	The Bused Timenig
938		The application of contrasting colored polymer (ink) onto
939		the surface of a tablet or capsule.
940		1
941	viii.	Laser Etching
942		
943		The application of identifying markings onto the surface of a
944		tablet or capsule using laser-based technology.
945		
946	ix.	Drilling
947		-
948		A drilling system typically is a custom built unit consisting of a
949		material handling system to orient and hold the solid dosage form,
950		a laser (or lasers), and optics (lenses, mirrors, deflectors, etc.) to

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			· · · · · ·
951			ablate the hole or holes, and controls. The drilling unit may include
952			debris extraction and inspection systems as well. The sorting,
953			orienting, and holding equipment commonly is provided by dosage
954			form printing equipment manufacturers, and is considered ancillary
955			in this use.
956			
957	2.	Equip	ment Classification
958			
959		a.	Pan Coating
960			
961			Pan coating subclasses primarily are distinguished by the pan configuration, the
962			pan perforations, and/or the perforated device used to introduce process air for
963			drying purposes. Perforated coating systems include both batch and continuous
964			coating processes.
965			
966			Conventional Coating System
967			Perforated Coating System
968			
969		b.	Gas Suspension
970			
971			Gas suspension subclasses primarily are distinguished by the method
972			by which the coating is applied to the substrate.
973			
974			Fluidized Bed with bottom spray mechanism
975			Fluidized Bed with tangential spray mechanism
976			Fluidized Bed with top spray mechanism
977			Fluidized Bed with Wurster column
978			Spray Congealing/Drying
979			spray congeaning/Drying
980		c.	Vacuum Film Coating
981		C.	vacuum 1 mm Couning
982			Although there may be differences in the jacketed pan, baffle system, or
983			vacuum source, no vacuum film coating subclasses have been identified.
984			vacuum source, no vacuum mm countig succiusses nave ceen identifica.
985		d.	Dip Coating
986		.	2.p commg
987			Because of the custom design associated with this class of coating, no dip
988			coating subclasses or examples have been identified.
989			coming coccination of committees have even recommittees.
990		e.	Electrostatic Coating
991			· · · · · · · · · · · · · · · · · ·
992			Because of the custom design associated with this class of coating, no
993			electrostatic coating subclasses or examples have been identified.
994			
995		f.	Compression Coating

997			Refer to the U	Jnit Dosi	ng section of this document.
998 999		g.	Ink-Based Pri	inting	
1000		۶.	IIIK Busea I II	mung	
1001			Ink-based prin	nting sub	classes primarily are distinguished by the method by which
1002			-	_	to a capsule or tablet surface.
1003					
1004			 Offset 		
1005			 Ink Jet 		
1006					
1007		h.	Laser Etching	(Printin	g)
1008			Č		
1009			Although lase	er etching	systems may differ from one another, no laser
1010			_	_	e been identified.
1011			C		
1012		i.	Drilling		
1013					
1014			The method of	of produc	ing the laser pulse that ablates the hole(s) is of no
1015			consequence	to the ph	ysical-chemical properties of the product. Therefore, no
1016			dosage form of	drilling e	quipment subclasses have been identified.
1017					
1018	V.	SUPA	C-SS INFOR	MATIO	N
1019					
1020		A.	Particle Size	Reducti	on/Separation
1021	1	D - C::	4:		
1022	1.	Defini	nons		
1023 1024		0	Unit Operation	me	
1024		a.	Omi Operano	1115	
1025			i.	Particle	Size Reduction: The mechanical process of breaking
1027			1.		s into smaller pieces via one or more size reduction
1028				_	hisms. The mechanical process used is generally referred to
1029				as milli	
1030				••• ••	
1031				a.	Particle - Either a discrete particle or a grouping of
1032					particles, generally known as an agglomerate.
1033					
1034				b.	Particle Size Reduction Mechanisms
1035					
1036					• Impact - Particle size reduction by applying an
1037					instantaneous force perpendicular to the particle
1038					and/or agglomerate surface. The force can result
1039					from particle-to-particle or particle-to-mill surface
1040					collision.
1041					
1042					 Attrition - Particle size reduction by applying
1043					force parallel to the particle surface.

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		Draft World Implementation
1044		
1045		 Compression - Particle size reduction by applying a
1046		force slowly (as compared to impact) to the particle
1047		surface toward the center of the particle.
1048		1
1049		 Cutting - Particle size reduction by applying a
1050		shearing force to a material.
1051		**************************************
1052	ii.	Particle Separation: Particle size classification according to particle
1053		size alone.
1054		SIZE MONE.
1055	b. Operating P	rincinles
1056	o. operating i	
1057	i.	Fluid Energy Milling: Particle size reduction by high-speed
1058		particle-to- particle impact and/or attrition (also known as
1059		micronizing).
1060		
1061	ii.	Impact Milling: Particle size reduction by high-speed mechanical
1062		impact or impact with other particles (also known as milling,
1063		pulverizing, or comminuting).
1064		
1065	iii.	Cutting: Particle size reduction by mechanical shearing.
1066		
1067	iv.	Compression Milling: Particle size reduction by compression stress
1068		and shear between two surfaces.
1069		
1070	v.	Screening: Particle size reduction by mechanically-induced attrition
1071		through a screen (commonly referred to as milling or
1072		deagglomeration).
1073		
1074	vi.	Tumble Milling: Particle size reduction by attrition, using
1075		grinding media.
1076		
1077	vii.	Separating: Particle segregation based on size alone, without any
1078		significant particle size reduction (commonly referred to as
1079		screening or bolting).
1080		
1081	2. Equipment Classific	cations
1082		
1083	 a. Fluid Energy 	y Mills
1084		
1085	Fluid energy	mill subclasses have no moving parts and primarily differ in
1086	the configur	ation and/or shape of their chambers, nozzles, and classifiers.
1087	_	
1088	 Fixed ta 	rget
1089	 Fluidize 	

• Loop and/or oval

1091	 Moving target
1092	Opposed jet
1093	Opposed jet with dynamic classifier
1094	Tangential jet
1095	
1096	b. Impact Mills
1097	•
1098	Impact mill subclasses primarily differ in the configuration of the grinding
1099	heads, chamber grinding liners (if any), and classifiers.
1100	
1101	• Cage
1102	Hammer air swept
1103	Hammer conventional
1104	 Pin or disc
1105	
1106	c. Cutting Mills
1107	
1108	Although cutting mills can differ in whether the knives are movable or fixed, and
1109	in classifier configuration, no cutting mill subclasses have been identified.
1110	
1111	d. Compression Mills
1112	
1113	Although compression mills, also known as roller mills, can differ in whether one
1114	or both surfaces move, no compression mill subclasses have been identified.
1115	
1116	e. Screening Mills
1117	
1118	Screening mill subclasses primarily differ in the rotating element.
1119	
1120	Oscillating bar
1121	 Rotating impeller
1122	 Rotating screen
1123	
1124	f. Tumbling Mills
1125	
1126	Tumbling mill subclasses primarily differ in the grinding media used and
1127	whether the mill is vibrated.
1128	
1129	Ball media
1130	Rod media
1131	 Vibrating
1132	
1133	g. Separators
1134	
1135	Separator subclasses primarily differ in the mechanical means used to
1136	induce particle movement.
1137	

			CentrifugVibratory	gal y or shaker
No	ote:	If a siı		equipment is capable of performing multiple discrete unit operations,
				for its ability to impact particle size or separation.
]	В.	Mixing	
	1. 1	Defini	tions	
		a.	Unit Operation	on
			Mixing. The	a magnishtation of montialog malative to one enother to achieve
			_	e reorientation of particles relative to one another to achieve r randomness. This process can include wetting of solids by a liquid
			-	rsion of discrete particles, or deagglomeration into a continuous
				ng and cooling via indirect conduction may be used in this operation
			1	hase mixing or stabilization.
			1	
		b.	Operating Pr	inciples
			i.	Convection Mixing, Low Shear: Mixing process with a repeated
				pattern of cycling material from top to bottom, in which dispersion
				occurs under low power per unit mass through rotating low shear
				forces.
			••	
			ii.	Convection Mixing, High Shear: Mixing process with a repeated
				pattern of cycling material from top to bottom, in which dispersion occurs under high power per unit mass through rotating high shear
				forces.
			iii.	Roller Mixing (Milling): Mixing process by high mechanical
				shearing action where compression stress is achieved by passing
				material between a series of rotating rolls. This is commonly
				referred to as compression or roller milling.
			iv.	Static Mixing: Mixing process in which material passes through a
				tube with stationary baffles. The mixer is generally used in
				conjunction with an in-line pump.
	•			
	<i>2. 1</i>	Equipi	nent Classific	ation
		0	Convection M	Mixers, Low Shear
		a.	Convection	viincis, Luw Siledi
			This group n	ormally operates under low shear conditions and is broken down by
				gn and movement. Design can also include a jacketed vessel to
			facilitate hea	-

1185		
1186		 Anchor or sweepgate
1187		• Impeller
1188		• Planetary
1189		·
1190	b.	Convection Mixers, High Shear
1191		
1192		This group normally operates only under high shear conditions. Subclasses are
1193		differentiated by how the high shear is introduced into the material, such as by a
1194		dispersator with serrated blades or homogenizer with rotor stator.
1195		
1196		• Dispersator
1197		• Rotor stator
1198		
1199	c.	Roller Mixers (Mills)
1200		
1201		No roller mixer subclasses have been identified.
1202		
1203	d.	Static Mixers
1204		
1205 1206 1207		No static mixer subclasses have been identified.
	NT . TC .	
1208		ngle piece of equipment is capable of performing multiple discrete unit operations,
1209	it has been ev	valuated solely for its ability to mix materials.
1210 1211	С.	Emulsification
1211	C.	Emuismeation
1212	1. Defini	tions
1214	1. Dejiii	
1215	a.	Unit Operation
1216		1
1217		Emulsification: The application of physical energy to a liquid system consisting of
1218		at least two immiscible phases, causing one phase to be dispersed into the other.
1219		
1220	b.	Operating Principles
1221		
1222		i. Low Shear Emulsification: Use of low shear energy using
1223		mechanical mixing with an impeller to achieve a dispersion of the
1224		mixture. The effectiveness of this operation is especially dependent
1225		on proper formulation.
1226		
1227		ii. High Shear Emulsification: Use of high shear energy to
1228		achieve a dispersion of the immiscible phases. High shear can
1229		be achieved by the following means:
1230		
1231		a. Stirring the mixture with a high speed chopper or
1232		saw-tooth dispersator.

		Draji -	— Not for implementation
1233			
1234		b. Pas	ssing the mixture through the gap between a high-
1235			ed rotor and a stationary stator.
1236		1	,
1237		c. Pas	ssing the mixture through a small orifice at high pressure
1238			lve- type homogenizer) or through a small orifice at high
1239			ssure followed by impact against a hard surface or
1240		<u> </u>	posing stream (valve-impactor type homogenizer),
1240		11	using sudden changes of pressure.
1242		Cat	sing studen changes of pressure.
1242	2. Eqi	uipment Classification	
1244	z. Lyi	upment Classification	
1245		a. Low Shear Emulsifiers	
1246			
1247		Although low shear emuls	sification equipment (mechanical stirrers or impellers)
1248		•	uid flow imparted to the mixture (axial-flow propeller or
1249			ubclasses have been defined.
1250		,,	
1251		b. High Shear Emulsifiers	
1252		S	
1253		Subclasses of high shear e	emulsification equipment differ in the method used
1254		to generate high shear.	1 1
1255		2	
1256		 Dispersator 	
1257		• Rotor stator	
1258		 Valve or pressure hon 	nogenizer
1259		1	e
1260	Note: If	a single piece of equipment is	capable of performing multiple discrete unit
1261			solely for its ability to emulsify materials.
1262	-		, , , , , , , , , , , , , , , , , , ,
1263	D.	Deaeration	
1264			
1265	1. Dej	finitions	
1266		a Unit Operation	
1267 1268		a. Unit Operation	
1269		Deaeration: The eliminat	ion of trapped gases to provide more accurate
1270			and remove potentially reactive gases.
1271		V 0.10.2220 2220 2220 2220 2220 2220 2220	and remove perentally reactive guides.
1272		b. Operating Principles	
1273		TTI C	
1274 1275			ative pressure, alone or in combination with mechanical
1275		intervention or assistance.	
1277	2. Eqi	uipment Classification	
1278	7	1	
1279		a. Deaerators	
1280			

Contains Nonbinding Recommendations Draft — Not for Implementation Deaerator subclasses differ primarily in their air removal paths, either through the bulk material or through a thin film, and in whether they use a batch or in-line process. Off-Line or in-line Vacuum vessel Note: If a single piece of equipment is capable of performing multiple discrete unit operations, it has been evaluated solely for its ability to deaerate materials. E. Transfer 1. Definition

a. Unit Operation

Transfer: The controlled movement or transfer of materials from one location to another.

b. Operating Principles

- i. Passive: The movement of materials across a non-mechanically-induced pressure gradient, usually through conduit or pipe.
- ii. Active: The movement of materials across a mechanically-induced pressure gradient, usually through conduit or pipe.

2. Equipment Classification

a. Low Shear

Active or passive material transfer, with a low degree of induced shear

- Diaphragm
- Gravity
- Peristaltic
- Piston
- Pneumatic
- Rotating lobe
- Screw or helical screw

b. High Shear

Active or mechanical material transfer with a high degree of induced shear

- Centrifugal or turbine
- Piston
- Rotating gear

Note: This section is intended to deal with the transfer of shear sensitive materials, including product or partially manufactured product. A single piece of equipment can be placed in either a low or high shear class, depending on its operating parameters. If a single piece of equipment is capable of performing multiple discrete unit operations, the unit has been evaluated solely for its ability to transfer materials.

1335				
1336		F.	Packaging	
1337				
1338	1.	Defini	tions	
1339				
1340		a.	Unit Operation	n
1341				
1342			i.	Holding: The process of storing product after completion of
1343				manufacturing process and prior to filling final primary packs.
1344			::	Transfers. The process of releasting bulls finished and dust from
1345 1346			ii.	Transfer: The process of relocating bulk finished product from
1340				holding to filling equipment using pipe, hose, pumps and/or other associated components.
1347				associated components.
1349			iii.	Filling: The delivery of target weight or volume of bulk finished
1350			111.	product to primary pack containers
1351				product to primary pack containers
1352			iv.	Sealing: A device or process for closing and/or sealing primary
1353 1354				pack containers following the filling process.
		_		
1355		b.	Operating Prin	nciples
1356				TT 11
1357			i.	Holding: The storage of liquid, semi-solids, or product
1358				materials in a vessel that may or may not have temperature
1359				control and/or agitation.
1360			::	Transfers. The controlled measurement on transfers of meetanicle
1361			ii.	Transfer: The controlled movement or transfer of materials from one location to another.
1362				from one location to another.
1363 1364			iii.	Filling: Filling operating principles involve several associated
1365			111.	subprinciples. The primary package can be precleaned to remove
1366				particulates or other materials by the use of ionized air, vacuum,
1367				or inversion. A holding vessel equipped with an auger, gravity, or
1368				pressure material feeding system should be used. The vessel may
1369				or may not be able to control temperature and/or agitation. Actual
1370				filling of the dosage form into primary containers can involve a
1371				metering system based on an auger, gear, orifice, peristaltic, or
1372				piston pump. A head-space blanketing system can also be used.
1373				piston pump. Tribud space chaintening system can also be used.
1374			iv.	Sealing: Primary packages can be sealed using a variety of
1375				methods, including conducted heat and electromagnetic
1376				(induction or microwave) or mechanical manipulation (crimping
1377				or torquing).
1378				
1379	2.	Equip	ment Classifica	tion
1380		1 1	v	
1381		a.	Holders	
1382				

1383 1384 1385	Although holding vessels can differ in their geometry and ability to control temperature or agitation, their primary differences are based on how materials are fed.
1386	
1387	• Auger
1388	• Gravity
1389	• Pneumatic (nitrogen, air, etc.)
1390	
1391	b. Fillers
1392	
1393	The primary differences in filling equipment are based on how materials
1394	are metered.
1395	
1396	• Auger
1397	• Gear pump
1398	 Orifice
1399	Peristaltic pump
1400	• Piston
1401	
1402	c. Sealers
1403	
1404	The differences in primary container sealing are based on how energy is
1405	transferred or applied.
1406	
1407	• Heat
1408	• Induction
1409	• Microwave
1410	Mechanical or crimping
1411	 Torque
1412	
1413	