IPAC-RS
International Pharmaceutical Aerosol Consortium on Regulation & Science

29 January 2026

Comments on USP <1664.1> Assessment of Leachables in Orally Inhaled and Nasal Drug Products

General Comments

1. Risk management principles should be referred to throughout and applied within the chapter. These should be aligned with ICH quality risk management approaches and concepts (i.e., ICH Q9), as well as recommendations in the existing regulatory guidance, e.g., FDA *Draft Guidance for Industry, Metered Dose Inhaler (MDI) and Dry Powder Inhaler (DPI) Drug Products--Quality Considerations* (April 2018). In line with risk-based approaches and concepts for orally inhaled and nasal drug products (OINDP), the chapter should clearly state in the Introduction that there is a large variation in leachables risk among OINDP, due to the large and growing variety of products and innovation that has and continues to occur. We recommend that the chapter include statements noting the difference in leachables related risk among MDIs (high risk), DPIs (very low risk), and products such as solutions and sprays, where risk level may be in a range between high and very low risk. Testing recommendations should then be based on risk level rather than a "one-size" fits all approach, based on highest risk.
2. Throughout the draft chapter, there appears to be very little relation to concepts, approaches, nuances and details of OINDP CMC regulation and science, its development and evolution over the last 30 years relevant to leachables, modern industry practice, or the existing critical and relevant regulatory guidelines for orally inhaled and nasal drug products including the FDA guidance, *Metered Dose Inhaler (MDI) and Dry Powder Inhaler (DPI) Drug Products--Quality Considerations* (April 2018) and *Nasal Spray and Inhalation Solution, Suspension, and Spray Drug Products—Chemistry, Manufacturing, and Controls Documentation.*
3. The new ICH Q3E guideline is/will be a critically important reference for this chapter. There should be alignment between the Q3E guideline (once finalized) and this standards chapter, especially regarding the implementation of a risk management approach.
4. The chapter should include text that allows the user to apply different approaches outside of those suggested in the chapter, if scientifically justified.
5. Please make sure to align the recommended SCT value to 1.5 µg/day. This value is currently proposed in ICH Q3E and is accepted by regulatory agencies. Threshold concepts and values should align with ICH Q3E and ICH M7.
6. Special case compounds: this section should be aligned with the Potency Classes proposed in ICH Q3E, including the Class 3 compounds.
7. Risk assessments for extractables are noted in <1663> but there is a need to link and reference the risk assessments within this chapter as this provides the basis for the leachable testing then undertaken (if the assessment indicates that an extractable is not likely based on the review/justification, then testing for the leachable would also not be likely)
8. Reference to and relevant applicability of ICH Q3D as well as USP <232> and <233> should be included.

9. The solvent systems and general manufacturing approach referred to in USP <665> and <1665> are not applicable to MDIs and DPIs. Text should be included to recognize this and more generally, the potential variety of OINDP for which <665> and <1665> will not be applicable. Additionally, current FDA guidance relevant for OINDP do not require leachables (or extractables) assessment of manufacturing components for OINDP.
10. Post approval changes made to container closure system should also be done within an ICH Q9 risk-assessment framework/process. This draft chapter only makes passing references to product changes rather than noting or referring to a cohesive risk management approach or reference to established risk management approaches relevant to lifecycle and change management. The chapter seems to be saying that all testing previously done would automatically need to be redone based on any change, rather than conducting a scientifically and risk-based subset of evaluations. Risk impact assessments are typically done to determine what tests should be applied for a given change(s).
11. There seems to be little to no distinction in the proposed chapter between target leachables and unknown leachables. We note that once a method is validated for target leachables, the AET no longer applies to that compound; it only applies to the unspecified compounds.

Specific comments related to these general comments follow in the next several pages.

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Specific Comments

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Throughout document	Estimated AETs are converted to final AETs by adjusting the estimated AET with an uncertainty factor (UF)	Re-insert the text on uncertainty factors from the previous 1664.1 version, or insert similar text into the 1664 chapter It will also be helpful to align text with ICH Q3E, once that regulatory guideline is finalized.	The text discussing uncertainty factors in the previous 1664.1 version was a helpful general guide for users in understanding what uncertainty factors are, why they are needed, and how they are established/could be applied for a method.
Introduction	Various definitions	Align with USP <5>	Definitions are redundant and should be aligned with the descriptions in USP <5>
Section 2.1	Nasal spray products, either multidose or unit dose, typically include the drug product, the container closure system, a pump, and an actuator. The container closure system for nasal sprays comprises a plastic container and other components (typically plastic) that are responsible for the formulation, metering, atomization, and delivery to the patient. Critical components include those that are in constant contact with the formulation (e.g. the container and dip tube) and components that are part of the liquid pathway during device actuation but do not permit quick evaporation of the residual surface liquid.	Nasal spray products, either multidose, bi-dose or unit dose typically include a container system for the drug product and an actuation system. The container closure system for nasal sprays is typically comprised of a plastic or glass container and other components for the storage of the product and actuation which are typically metallic, plastic, and elastomeric in nature. Critical components include those that are in constant contact with the formulation (e.g. the container, dip tube and elastomeric closures) and, in the case of multi-dose, the components that are part of the liquid pathway during device actuation but do not permit quick evaporation of the residual surface liquid.	The terms do not include a wide enough scope of thought – it is written from the viewpoint of multi-dose and multiple container closures are used, not just plastic; therefore, suggested text expands to cover a greater range of materials that may be used.

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Section 3	Reference to 2-4	Change to reference 1-3	Seems to be a typo in the reference being made
Section 4.1	"the risk for liquid dosage forms… is high"	Revise to read: "…the risk for liquid dosage forms… is higher than for solid dosage forms, especially when organic solvents are included in the formulation."	As stated later in this section, aqueous formulations have a relatively low leaching potential.
Section 4.1	For regulatory submissions, OINDP's typically require…. (numerous bullet points below this text)	Align with quality risk management (QRM) approach as outlined in ICH Q9 and the workflow as presented in draft ICH Q3E guidance	Current section doesn't discuss a QRM based approach.
Section 4.1	For regulatory submission, OINDPs typically require: ….	Please clarify that for regulatory submissions, in addition to the leachables studies listed in this chapter, extractables information and a leachables and extractables correlation are recommended.	
Section 4.1	A leachables stability study for drug product registration that supports intended storage and use conditions throughout the proposed shelf-life (see Table 1 for **the proper** testing schedule),..	See Table 1 for **an example** testing schedule	Other approaches to stability may be justified. Text above Table 1 refers to an "example of stability storage conditions and testing time points". Intermediate testing at 30C/65% RH may not be warranted in all cases. We also strongly suggest that USP not use editorializing or moralizing language such as "proper."
Section 4.1	2nd bullet "sensitive, selective and fully validated leachable analytical methods"	Change the wording to: "Sensitive, selective and appropriately qualified leachable analytical methods"	If running non-targeted methods – the requirement of "fully validated" can't be met. Additionally, it may not be necessary to quantitatively

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			validate a method, where a limit test validation may be suitable.
Section 4.1	Although a safety concern threshold (SCT) of 0.15 µg/day and a qualification threshold (QT) of 5 µg/day total daily intake (TDI) for an individual organic leachable were previously published in the Product Quality Research Institute's OINDP best practices (4), current regulatory practice is an SCT of 1.5 µg/day.	A safety concern threshold (SCT) of 1.5 µg/day and a qualification threshold (QT) of 5 µg/day total daily intake (TDI) is in line with current regulatory practice.	Align with draft ICH Q3E guidance regarding SCT. It is confusing to reference the PQRI best practice document in this particular instance. These proposed revisions add clarity to the SCT value and confirms the appropriate QT value.
Section 4.1	"Applicants are recommended to consult with regulatory agencies before leachables and extractables studies are performed…"	Please clarify that a consultation is not necessary in any case but is recommended if deviating from standard procedures as described, e.g., other USP chapters, PQRI, and ICH.	Alignment with other industry practice documents, regulatory guidelines, and standards
Section 4.1	For liquid dosage forms: Complete qualitative and quantitative leachables–extractables correlations (which require that extractables assessments be accomplished on all critical packaging components; see *Assessment of Extractables Associated with Pharmaceutical Packaging/Delivery Systems* ⟨1663⟩.	Revise to: Where applicable (i.e., leachables presence are demonstrated in finished product): Complete qualitative and quantitative leachables–extractables correlations (which require that extractables assessments be accomplished on all critical packaging components; see *Assessment of Extractables Associated with Pharmaceutical Packaging/Delivery Systems* ⟨1663⟩).	For aqueous based drug product, leachables may not be detected at levels greater than the AET, and therefore correlation can only be performed when leachables are greater than the AET.
Section 4.1	For liquid dosage forms: Leachables specifications including acceptance criteria (assumes a complete extractables assessment for each critical packaging component). (Note that in some cases,	For liquid dosage forms: Leachables specifications including acceptance criteria, assuming the complete extractables assessment for each critical packaging component. Note that, in case a comprehensive leachables to extractables	Rephrased for a better alignment with PQRI guideline for OINDP.

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	routine extractables testing for release of critical components can be used to control drug product leachables in lieu of routine drug product leachables testing, providing that a comprehensive leachables–extractables correlation is established)	correlation is established, it is possible to use routine extractables release testing to control drug product leachables, in lieu of routine drug product leachables testing.	
Section 4.1	For liquid dosage forms: Leachables specifications including acceptance criteria (assumes a complete extractables assessment for each critical packaging component).	Only relevant if leachables are observed over the AET	As noted in other comments above, only relevant if leachables are observed over the AET
Section 4.1	For **drug products** packaged in semipermeable containers (e.g., low density polyethylene) without protective packaging that are intended for storage under controlled room temperature conditions, and, drug products intended for storage in a refrigerator, refer to *FDA's Guidance for Industry: Nasal Spray and Inhalation Solution, Suspension, and Spray Drug Products—Chemistry, Manufacturing, and Controls Documentation*	For **nasal spray, inhalation solution, suspension and spray drug products** packaged in semipermeable containers (e.g., low density polyethylene) without protective packaging that are intended for storage under controlled room temperature conditions, and drug products intended for storage in a refrigerator, refer to *FDA's Guidance for Industry: Nasal Spray and Inhalation Solution, Suspension, and Spray Drug Products—Chemistry, Manufacturing, and Controls Documentation*	The FDA guidance referred to in this section states: 'This guidance does not address propellant-based inhalation and nasal aerosols (also known as oral and nasal metered dose inhalers, MDIs), inhalation powders (also known as dry powder inhalers, DPIs), and nasal powders',
Section 4.1 Table 1	…for OINDP…not packaged in semipermeable containers	Delete “not packaged in semipermeable containers”.	It is not clear, why these conditions should not be suitable for DP packaged in semipermeable containers.
Section 4.1 Table 1	[Table 1, Left-hand column of temperatures and RH values]	Remove the middle set of conditions	There does not seem to be a rationale for adding a 3rd set of

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			conditions when there is only 5°C difference. Very unclear what additional data is gained by this.
Section 4.2	For the actuator, this includes contact parts (such as the sump, actuator orifice, and mouthpiece) and noncontact parts (such as the sleeve for the canister).	Suggest to remove 'For the actuator, this includes contact parts (such as the sump, actuator orifice, and mouthpiece) and noncontact parts (such as the sleeve for the canister).' as the threshold for actuators is 20 µg/g.	Contradicts later sentence of 'Although it is unlikely to contribute leachables to the emitted drug product aerosol plume, potential patient exposure to chemical entities from the MDI plastic actuator or mouthpiece should be assessed at a threshold of 20 µg/g (see ⟨1663⟩).'
Section 4.2	…potential patient exposure to chemical entities from the MDI plastic actuator or mouthpiece should be assessed…	Add "extractables" to "chemical entities"	Leachables are tested on DP contact parts, parts not in contact with the DP but in contact with patient like mouthpieces are tested for extractables.
Section 4.2	"Additional studies and references are required to assess….including references to indirect food additive regulations and…"	Delete this requirement related to indirect food additive regulations	Although the information might be supportive it is neither required for OINDPs as of USP chapters 661.1 and 661.2, nor is it sufficient.
Section 4.2	Applicants should describe a control strategy that ensures the continued reproducibility of the delivery system. For example, if constructed from materials acceptable for food contact, MDI actuators and mouthpieces, "spacers", and other components and devices specified in the	Applicants should describe a control strategy that ensures the continued reproducibility of the delivery system. ~~For example, if constructed from materials acceptable for food contact, MDI actuators and mouthpieces, "spacers", and other components and devices specified in the drug product labeling generally may only need to be~~	Proposed to remove the noted text so that the recommendation aligns with the FDA Guidance for industry Table 7, which states that control extraction procedure and data are not required for

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	drug product labeling generally may only need to be appropriately characterized (i.e., extraction studies and possibly routine extractables testing) to ensure continued consistent composition of the component or device.	~~appropriately characterized (i.e., extraction studies and possibly routine extractables testing) to ensure continued consistent composition of the component or device.~~	actuator/mouthpiece and additional accessories.
Section 4.2	'4. Development and validation of extractables profile release tests for the incoming actuators or mouthpieces, with appropriate qualitative and quantitative acceptance criteria.'	Remove this entire sentence	Propose to remove so the recommendation aligns with the FDA Guidance for industry Table 7, which states that Control extraction procedure and data are not required for actuator/mouthpiece and additional accessories.
Section 4.2	Any post-approval changes (for example, material, dimensions, or source of supplier) made to the container closure systems of MDIs require repetition of the above recommendation to establish that the changed systems conform to relevant quality standards.	Any post-approval changes (for example, material, dimensions, or source of supplier) made to the container closure systems of MDIs would require a risk-based review to determine the potential impact of the data already generated.	Align with the ICH Q9 risk-based approach.
Section 4.3	Applicants should describe a control strategy that ensures the continued reproducibility of the delivery system.	Applicants should describe a control strategy that ensures the continued reproducibility of the delivery system where leachables are observed at greater than 30% of the PDE.	Requirement for a control strategy should be dependent on risk, i.e., if leachables are observed and present a concern, therefore a control strategy is required. Propose wording aligns with ICH M7 and ICH Q3D.
Section 4.3	When constructed from materials acceptable for food contact, nasal spray	When constructed from materials acceptable for food contact, nasal spray critical components not in	If routine extractables testing is not required for MDI, then it would be

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	critical components not in continuous contact with the drug product formulation may only need to be appropriately characterized (i.e., extraction studies and possibly routine extractables testing) to ensure a consistent composition of the component.	continuous contact with the drug product formulation may only need to be appropriately characterized (i.e., extraction studies) ~~and possibly routine extractables testing) to ensure a consistent composition of the component~~.	assumed that also not appliable for nasal sprays
Section 4.3	In addition, based on applicable regulatory guidance, drug product applicants should consider the following (see ⟨1663⟩): Development and validation of extractables release tests for incoming container closure and pump critical components, with appropriate qualitative and quantitative acceptance criteria.	In addition, based on applicable regulatory guidance, drug product applicants should consider the following *when potential safety risk has been identified:* (see ⟨1663⟩): Development and validation of extractables release tests for incoming container closure and pump critical components, with appropriate qualitative and quantitative acceptance criteria.	This revision will help align the text with a risk-based approach and eliminate unnecessary testing which has no impact on patient safety.
Section 4.4	Leachables in inhalation sprays should be characterized (i.e., identified and quantitated) at levels above a calculated AET. An AET can be calculated for any OINDP dosage form by applying the OINDP SCT (i.e., 1.5 µg/day for an individual organic leachable)."	Propose to add the following (noted in red font): "Because inhalation sprays are typically aqueous-based formulations, and the vast majority of potential organic leachables are relatively lipophilic with low aqueous solubility, the risk of formulation–packaging component interaction is lower than that for organic propellant-based MDIs. Leachables in inhalation sprays should be characterized (i.e., identified and quantitated) at levels above a calculated AET. An AET can be calculated for any OINDP dosage form by applying the OINDP SCT (i.e., 1.5 µg/day for an individual organic leachable)."	Accurately reflect that inhalation spray products are not as high a risk as MDI, but greater risk than DPIs.

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Section 4.4	Estimated AET = (45 µg/day ÷ container) x (1 container/0.4 g)	Estimated AET = (45 µg/container) x (1 container/0.4 g)	Think the formula may have an error as the suggested amend makes more sense (as unsure where 45 µg/day comes from to include in the equation)
Section 4.4	Consideration of validated tests for probable leachables from labels, inks, adhesives, etc., with appropriate acceptance criteria, if such tests are appropriate and applicable.	Propose to remove this sentence and add the below to the introduction of Section 4.4.: "Leaching can potentially occur from the unit dose container (e.g., LDPE), which is in long-term continuous contact with the drug product formulation. It is also possible that organic chemical entities associated with paper labels, adhesives, and inks, in direct contact with the permeable unit dose container, can migrate through the container and into the formulation. Leachables from tertiary packaging systems (e.g., cardboard shipping containers) are also possible."	This is justifiable with respect to a risk-based approach to leachables and is in line with global regulatory guidance (from regulatory agencies, including the FDA)
Section 4.5	An appropriate control strategy should be developed to ensure reproducibility of packaging materials.	An appropriate control strategy should be developed, when safety concern (leachables at greater than 30% of PDE) have been identified during the development phase, to ensure reproducibility of packaging materials. Alternatively, remove the entire original sentence.	Aligns with a risk-based approach and ICH M7 and ICH Q3D.
Section 4.5	Potential patient exposure to chemical entities from inhalation solution, suspension, and spray critical components not in continuous contact with the drug	Remove one instance of this sentence	This sentence is duplicated in the draft

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	product formulation should be assessed at a threshold of 20 µg/g (see ⟨1663⟩)		
Section 4.5	If constructed from materials acceptable for food contact, inhalation solution, suspension and spray critical components not in continuous contact with the drug product formulation generally may only need to be appropriately characterized (i.e., extraction studies and possibly routine extractables testing) to ensure continued consistent composition of the component.	If constructed from materials acceptable for food contact, inhalation solution, suspension and spray critical components not in continuous contact with the drug product formulation generally may only need to be appropriately characterized (i.e., extraction studies) ~~and possibly routine extractables testing) to ensure continued consistent composition of the component.~~	If routine extractables testing is not required for MDIs, then it would be assumed that it is also not appliable for inhalation solutions and suspensions
Section 4.6	General text for section	Recommend to align with FDA guidance and state the volatile/semi-volatile leachables are only required for DPIs.	FDA guidance for industry MDI and DPIs states that for DPIs, volatile/semi-volatile leachables content should be assessed: reference to line 169 of the FDA guidance.
Section 4.6	An AET can be calculated for any OINDP dosage form by applying the OINDP SCT (i.e., 0.15 µg/day for an individual organic leachable).	An AET can be calculated for any OINDP dosage form by applying the OINDP SCT (i.e., 1.5 µg/day for an individual organic leachable).	The example below this sentence uses an example with 1.5 µg/day, therefore we believe this number is a typographical error and should be 1.5 rather than 0.15 Alignment with rest of the chapter
Section 4.6	When constructed from materials acceptable for food contact, the inhalation powder packaging system and DPI device critical components not in continuous	When constructed from materials acceptable for food contact, the inhalation powder packaging system and DPI device critical components not in continuous contact with the drug product	Align with FDA Guidance for industry for metered dose inhalers and DPIs, Table 7.

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	contact with the drug product formulation generally only need to be appropriately characterized (i.e., extraction studies and routine extractables testing) to ensure a continued consistent composition of the component.	formulation generally only need to be appropriately characterized (i.e., extraction studies) ~~and routine extractables testing) to ensure a continued consistent composition of the component.~~	
Section 4.6	In addition, for DPIs and inhalation powders, and based on applicable regulatory guidance (2), if leachables with safety concerns are identified, drug product applicants should consider the following (see ⟨1663⟩): Development and validation of extractables release tests for relevant incoming inhalation powder packaging systems and critical components of DPI devices, with appropriate qualitative and quantitative acceptance criteria.	Propose to remove this text.	Justified based on aligning with the FDA Guidance for industry for metered dose inhalers and DPIs, Table 7, which states that control extraction procedure and data are not required for Device Constituent Part and Components.
Section 4.7	Analysis of N-nitrosamines as leachables in MDI drug products using GC-TEA has been reported (7)	Remove or include a current, relevant reference	Reference 7 is not relevant to MDIs as this is specific to baby bottle rubber nipples. Please clarify this – how can the reference be reporting MDI if testing a baby bottle rubber – please clarify and update reference or remove reference.
Section 4.7	GC-TEA is suggested as an analytical method for nitrosamines.	Refer to state-of-the-art analytical test methods like GC-MS or LC-MS.	There are better, state-of-the-art analytical test methods available like GC-MS or LC-MS.

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Section 4.8 Elemental Impurities	Elemental impurities may be present in OINDPs as a result of their interaction with packaging systems. Packaging and critical packaging components for OINDPs should be tested for extractable elements, and OINDPs should be characterized over their shelf life for elemental impurities, consistent with the requirements and guidelines contained in International Council for Harmonisation (ICH) Q3D (10).	Elemental impurities may be present in OINDPs as a result of their interaction with packaging systems. A risk-based approach, consistent with the requirements and guidelines contained in International Council for Harmonisation (ICH) Q3D, should be applied. USP <232> and <233> can also be considered.	There is no reference to USP <232> and <233>. We request to add these USP chapter references for elemental impurities. The proposed revision provides better clarity and integration of guideline references. This also simplifies the statement and clarifies that the guidance of importance for E&L is ICH Q3D, and also reminds the reader of <232> and <233>. Also note that although reference is made to ICH Q3D, the current text contradicts that guideline by stating that elemental impurities should be characterized over shelf life. Elemental impurities can be sourced from API, excipients, etc., (as detailed in the FDA guidance for industry for metered dose inhalers and dry powder inhalers) and methods used to assess elemental impurities are unable to distinguish the source of the impurities as leachables from the CCS. Consider removing this section, if not making the revision noted above.

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Section 5	Metallic, glass, or ceramic components used to manufacture OINDPs do not require qualification for organic extractables, as such components are not sources of organic extractables or leachables. The risk of such components leaching elemental impurities into OINDPs must be assessed. Assessments that conclude that there is a high risk of leaching of elements must be followed by appropriate extractables or leachables testing. If extractables testing does not reveal extracted elements in excess of the appropriate control threshold [e.g., 30% of the element's permitted daily exposure (PDE)], then testing manufactured drug products for manufacturing-related leached elements is not required.	Propose to remove all of this text.	Risk assessment and testing of *finished product* in accordance with ICH Q3D would mitigate the requirement for performing extractables testing on the manufacturing components. This discussion must thus clearly refer to *finished product elemental impurities* testing, not leachables testing on manufacturing components. Leachables testing is used to assess the risk to the patient; the patient is exposed to the finished product and not the manufacturing equipment.
Section 5	Plastic components used to manufacture OINDPs, or their relevant materials of construction, must be well characterized: • The manufacturing system itself, or all of its relevant materials of construction, complies with the relevant compendial monographs. • The manufacturing system itself, or all of its relevant materials of construction, complies with the relevant food contact safety	Propose to remove all of this text.	The compendial monograph is the USP <665>, which isn't compulsory or official *or representative of the manufacturing process of MDIs or many other OINDP* *Additionally, there is no requirement for assessment of the manufacturing components in the FDA guidance for MDI and DPI or FDA guidance for nasal spray and inhalation solution, suspension and spray drug products.*

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	regulations (e.g., 21 CFR 174–186) and compliance is adequately justified (e.g., proposed use is consistent with regulations for food contact use, the leaching propensity of the OINDP process stream is similar or less than the extraction solvent(s) listed in a referenced regulation, and all specified testing results for the manufacturing system or material meet the specified acceptance criteria).		Testing of finished product would also be representative of the manufacturing process, and therefore 'qualify' the equipment. Leachables testing is used to assess the risk to the patient; the patient is exposed to the finished product and not the manufacturing equipment.
Section 5	For plastic OINDP manufacturing components, the risk of such components leaching organic impurities into OINDPs must be assessed. If the assessments conclude that the risk is high, appropriate extractables or leachables testing must follow. Depending on the outcome of extraction studies, leachables studies may also be required on a case-by-case basis. *Plastic Components and Systems Used to Manufacture Pharmaceutical Drug Products and Biopharmaceutical Drug Substances and Products* ⟨665⟩ and *Characterization and Qualification of Plastic Components and Systems Used to Manufacture Pharmaceutical Drug Products and Biopharmaceutical Drug Substances and*	Propose to remove all of this text.	Solvents selected in <665> are not representative of MDI (or in many cases, other OINDP types) manufacturing processes. Furthermore, it is not a requirement to assess manufacturing components within the FDA guidance for MDI and DPI or FDA guidance for nasal spray and inhalation solution, suspension and spray drug products. Leachables testing is used to assess the risk to the patient; the patient is exposed to the finished product and not the manufacturing equipment.

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	Products ⟨1665⟩ should be consulted to facilitate the design and implementation of any necessary extractables and leachables studies for plastic manufacturing components.		