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International Pharmaceutical Aerosol Consortium on Regulation and Science

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1 December 2014

Dr. Desmond Hunt
United States Pharmacopeial Convention
12601 Twinbrook Parkway
Rockville, MD 20852-1790 USA

Dear Dr. Hunt,

On behalf of the International Pharmaceutical Aerosol Consortium on Regulation and Science (IPAC-RS), please find enclosed comments on USP chapters <661>, <661.1>, and <661.2>. We thank the USP for developing recommendations to assist industry in providing quality products to patients, and appreciate this opportunity to comment on these documents.

As an international consortium of innovator and generic companies that develop, manufacture, and market orally inhaled and nasal drug products for the treatment of diseases such as asthma, chronic obstructive pulmonary disease, and diabetes, IPAC-RS is committed to advancing consensus-based, scientifically driven standards and regulations for inhalation products, with the purpose of facilitating the availability of high-quality, safe, and efficacious drug products to patients.

We provide here, general comments to the chapters. The tables following these contain specific comments, many of which provide examples related to these general comments.

- The recommendations and requirements included in these documents are not appropriate for a range of diverse drug product types including, e.g., inhalations and solid orals. Overall, the chapters do not reflect consensus documents that provide guidance useful for many product types.
- The chapters are not written within a risk-based approach framework, nor does it appear that any risk-based concepts have been applied to specific sections/requirements. For example, the chapters do not recommend minimum requirements with the flexibility to adhere to more rigorous requirements based on the drug product and route of administration. Indeed, in many instances, the chapters appear to present quite rigorous and rigid standards with little or no flexibility to reduce, streamline, or enhance testing approaches based on scientific justification, including knowledge of the drug product profile and manufacturing processes, and supplier information. Specific examples, among many, include (i) the concept that extractables studies should be performed in a manner that is appropriate to the dosage form and its route of administration (e.g., solvent selection, need for simulation studies); and (ii) the product specific determination of the need for in vivo biocompatibility testing via <88> in addition to toxicological assessment of individual leachables and/or extractables).
- The chapters do not appear to address packaging (and/or container closure system) component testing, which is a common approach used for many drug products, including

inhalation drug products. It would be helpful to clarify recommendations related to finished component testing.

- The drafts do not seem to be aligned with ongoing international harmonization activities, e.g., ICH.

Please also consider including, perhaps in <661>, an explanation of the USP process for how these chapters will (or will not) be applied to existing products and specifications. We believe such explanation will be very helpful to pharmaceutical manufacturers.

We are happy to discuss these further with you directly, and/or provide further information if needed.

Sincerely,

Susan Holmes, GlaxoSmithKline
Chair, IPAC-RS Board of Directors

Robert Berger, Merck & Co
Vice-Chair, IPAC-RS Board of Directors

IPAC-RS Comments to USP Chapters <661>; <661.1>, <661.2>

<661> Plastic Packaging Systems and Their Materials of Construction

<661> Section and/or Para	*USP Text*	Comment	Suggested Revision or Consideration for USP
General		It is not clear the extent of testing necessary for different products (intended use), This should be addressed in the general overview.	Clarify that some tests are only applicable for high risk products and products with a high likelihood of packaging component-dosage form Interaction such as ophthalmic, parenteral, and inhalation products and not for solid oral products.
General		It would be helpful if the chapter provided a reference to chapter(s) dealing with labels, inks, and adhesives which can also contribute leachables.	Consider providing reference to chapter(s) dealing with labels, inks, and adhesives which can also contribute leachables.
General		The chapter only addresses potential leachables, it would be helpful for the chapter to also point to performance testing suggestions.	Consider including performance testing suggestions or references
Overall concept (see Scope)	*Testing of these plastic materials of construction to establish that they are well characterized and suitable for use in packaging systems is within the scope of this series of chapters*	The overall concept presented here seems to be that all materials of construction, regardless of intended use, must undergo all testing that is really only appropriate for high risk products. This results in either excessive testing or a smaller pool of materials to chose from or both. There should be a minimum set of criteria that all packaging materials of construction should meet (e.g., food contact compliance) and tests added as the risk associated with route of administration and interaction likelihood increases.	We suggest that risk-based approaches are encouraged and highlighted in the introductory text. Reference can also be made to the risk and likelihood of interaction table by dosage forms from the new <1664> chapter. We appreciate that specifications need to be met for materials, but how it is demonstrated that specifications be met should be based on a scientific approach to the intended use and based on the type of risk involved. This may involve obtaining information from suppliers or experimental testing.
Overall concept (see	*Testing of packaging systems to establish that they are suited for*	Being suitable for intended use ultimately is proven by product testing on stability. Suitability	Suggested rewrite: Testing of packaging systems, or their

<661> Section and/or Para	*USP Text*	Comment	Suggested Revision or Consideration for USP
Scope)	*their intended uses is within the scope of this series of chapters*	for use as a pharmaceutical packaging system could potentially be established with the 661 tests but the system and intended use suitability can only be finally determined by product testing. In some cases it may not be feasible to experimentally test the entire packaging system until it contains product. Testing of individual components may be necessary and in some cases beneficial to understand where is the highest chemical risk. Component testing should not be omitted as an option.	components, to establish that they meet general safety criteria is within the scope of this series of chapters.
Introduction (terminology)	*Systems constructed from plastic materials and components are used to package therapeutic products…* *Such systems and their associated materials and components of construction are considered and defined in Packaging and Storage Requirements 659. The plastics used in packaging systems are composed of homologous polymers…* *Such contact may result in an interaction between the therapeutic products and the packaging systems and its materials or components of construction.* *Obtaining such a necessary and desirable outcome is facilitated by the use of well-characterized plastic materials of construction in*	There are several terms that we strongly believe are not used appropriately: In USP <659> the definition of a packaging system is the sum of the packaging components, which are described as including containers, container liners, closures, ferrules, overseals, closure liners, inner seals, administration ports, overwraps, administration accessories and labels. There are no "components of construction," only "materials of construction." Additionally not all packaging is made from homologous polymers	Suggest rewriting statements using the appropriate terms: "Systems made from components are used to package therapeutic products…" "Such systems and their associated materials of construction are considered and defined in *Packaging and Storage Requirements* 659. The plastics used in packaging system components are composed of polymers…" "Such contact may result in an interaction between the therapeutic products and the packaging systems and its materials of construction." "Obtaining such a necessary and desirable outcome is facilitated by the use of well-characterized plastic materials of construction in components, and by the appropriate testing of packaging systems."

<661> Section and/or Para	*USP Text*	Comment	Suggested Revision or Consideration for USP
	components, containers, and packaging systems and by the appropriate testing of packaging systems.		
Scope	*Establishing the suitability of plastic packaging systems*	The material selection process starts with evalution of suppliers' information like indirect food contact approval. A second step for high risk products, such as injectables and inhalation drug products would be a material characterization (extractables study). Table 2 "Typical Suitability Considerations for Common Classes of Drug Products" of the FDA Guidance for Industry: Container Closure Systems for Packaging Human Drugs and Biologics, 1999, regarding safety should be considered.	Suggest adding a bullet, with respect to establishing suitability, e.g., *As appropriate, reference to the indirect food additive regulations.*
Scope	*Material screening: Characterization of a packaging system's materials of construction to evaluate ingredients as probable extractables and tentative leachables.*	The overall intent of this statement seems to be about understanding material composition. Extractables testing is one way to obtain such information. Supplier information on material formulation and processing is another. The experimentation outlined does not give probable but actual extractables - remove "probable" The term "potential leachables" has been used for many years to describe what is here listed as "tentative leachables" - this term creates an incorrect impression - "potential" indicates that they could be, tentative indicates that they are until proven otherwise, which could lead to incorrect assumptions by reviewers of data	Suggested rewrite: Characterization of a packaging system's materials of construction to evaluate ingredient composition.
Scope	*Controlled extraction (simulation) study: Worst-case controlled extraction (simulation) study to*	The text appears to be equating simulation studies with Controlled Extraction Studies – these are not equivalent and should not be	Suggest the following revision: A Controlled Extraction Study - a laboratory investigation into the qualitative and quantitative

<661> Section and/or Para	*USP Text*	Comment	Suggested Revision or Consideration for USP
	determine the extent to which extractables may become probable leachables	suggested to be so. Simulation is not worst case - aggressive extraction conditions would be worst case - this needs to be changed because it is in direct conflict with the PQRI recommendations where controlled extraction is under aggressive conditions Simulation studies could be considered a subset of controlled extraction studies, but is not a worst case study.	nature of extractables profiles of components of a container/closure system with the purpose to systematically and rationally identify and quantify potential leachables, i.e., extractables.
Scope	*Assembled packaging systems are filled to contain the therapeutic product by various means and at various points in the packaging system manufacturing process*	What about API and excipient containers; bulk therapeutic product storage; and polymeric coatings?	Consider indicating whether these are in (or out of) scope

<661.1> Plastic Materials of Construction

<661.1> Section and/or Para	USP Text	Comment	Suggested Revision or Consideration for USP
Introduction	*For the purposes of this chapter, a plastic material of construction is deemed to be well-characterized for its intended use if the following characteristics have been adequately established: its identity, biocompatibility (biological reactivity), general physicochemical properties, and composition (i.e., additives and extractable metals likely to be present).*	The use of extractable additives and metals tests for oral solids would be excessive. The definition of well-characterized here seems to have been taken from parenteral products and applied to all drug product types. Extractable metals criteria include many metals that would not be of safety concern and not part of a performance requirement. On the other hand, it would have been expected that materials should have a heavy metals specification for As, Pb, Cd or Cr(VI), yet there is no mention of these.	We recommend that the minimum for well characterized materials be identity, and that using a risk-based approach – depending on the knowledge of the route of administration, drug product type, etc. -- other composition aspects can be tested for. Consider including specifications focused on metals of safety concern.
Introduction	*Because chemical testing alone may not be adequate to establish a material's suitability for use, chemical testing is augmented by the orthogonal approach of establishing biological reactivity.*	Biological reactivity tests are designed for finished components not materials. Extractables testing on a material will not pick up any additives that are used during fabrication. The testing rationale stated in ISO 10993 is that extractables characterization is used to guide which biocompatibility tests are to be performed. Extractables characterization is more suitably performed on components. In other words, establishing a material's suitability for use can only be done by testing that material in its finished form – a fabricated component or packaging system.	Biological reactivity can be used along with chemical testing as supportive data for selection of materials for high risk drug products (OINDP, PODP). However, the final determination of suitability for use in a specific drug product involves a safety qualification process using extractables and leachables data to assess the safety of the material for its intended use.
Scope	*This chapter solely applies to individual plastic materials and should not be applied to*	The chapter specifically excludes multilayer *structures* but does not specify how to address multiple layer *materials*	Consider providing some input regarding handling of multiple layer materials; or a statement that such materials are not within scope.

<661.1> Section and/or Para	USP Text	Comment	Suggested Revision or Consideration for USP
	packaging systems or components consisting of multiple individual plastic materials		
Scope	*Polyethylene, polyolefins, polypropylene…*	Polyolefins are primarily thought of as polyethylene and polypropylene (see any polymer handbook on the topic). Therefore the use of the term "polyolefins" is redundant. This term does not adequately represent what is detailed in the section titled "polyolefins"	Consider changing this term to be "cyclic olefin copolymer" throughout the document
Scope	*Specifically, the unaddressed material of construction must be identified by appropriate methodology and tested for biocompatibility, physicochemical properties, additives, and relevant extracted metals.*	See comments on additive, heavy metal, and biocompatibility testing for introduction	
Table 1 Guidelines for Application of Tests *Oral Tablets, Oral Hard and Soft Gelatin Capsules, Oral Powders, and Topical Powders*	*Perform Biological Reactivity tests, in vitro <87>* *Components that meet the requirements of these tests do not need to undergo testing as described in In Vivo< 88>* *AND* *Perform Identification, Physicochemical, Extractable Metals, and Plastic Additives tests as*	This table states that the testing requirements for orals are largely no different than for other dosage forms, e.g., overall there are no differences between oral and other dosage forms except for the In Vivo (<88>) testing. This does not reflect a risk-based approach; in many cases performing extractables testing is not needed. Furthermore, tests noted in the material specific sections are not dosage form specific and therefore the table instruction loses its meaning. The recommended extent of testing seems to not be appropriate for orals, which should only consider description of the material, identification of the material, and characteristic properties, e.g., mechanical, physical parameters, heavy	Revise to include the concepts: For Topical Delivery Systems, Topical Solutions and Suspensions, and Topical and Lingual Aerosols, Oral Solutions and Suspensions: Typically, an appropriate reference to the indirect food additive regulations is sufficient for drug products with aqueous based solvents. Drug products with non-aqueous based solvent systems or aqueous based systems containing co-solvents generally require additional suitability information. For Topical Powders, Oral Powders Oral Tablets and Oral (Hard and Soft Gelatin) Capsules: Typically, an appropriate reference to the indirect food additive regulations is sufficient.

<661.1> Section and/or Para	USP Text	Comment	Suggested Revision or Consideration for USP
	directed for these dosage forms	metals and nonvolatile residue. Note also that the EMA guideline on plastic immediate packaging materials does not require more testing for oral drug products than for foodstuffs Finally, the requirements do not reflect Table 2 "Typical Suitability Considerations for Common Classes of Drug Products" in the FDA Guidance for Industry: Container Closure Systems for Packaging Human Drugs and Biologics, 1999, regarding safety, where reference to appropriate indirect food additive legislation is sufficient.	More specifically, should also revise Chemical Tests entry to read: Perform *Identification, Physicochemical* tests. Remove *"as directed for these dosage forms."* Reduce physicochemical testing (for orals) to heavy metals and nonvolatile residue. Delete any unspecific testing like absorbance, acidity or alkalinity, TOC. Delete plastic additives testing for low risk drug products, where reference to foodstuff regulations is appropriate.
Table 1 Guidelines for Application of Tests *Oral Tablets, Oral Hard and Soft Gelatin Capsules, Oral Powders, and Topical Powders*	*Materials that do not meet these requirements are not suitable for packaging for these dosage forms*	The list of allowed additives does not represent all materials used, especially for oral drug products. For orals, all additives with indirect food additive approval should be allowed Further this requirement does not reflect what is described in the text preceding Table 1: "Alternatively, unaddressed materials may, in justified circumstances, comply with other specifications, subject to approval by an appropriate regulatory authority."	Suggest that this statement should not be applicable to low risk drug products, e.g., oral drug products. May be better to make a third column for low risk products Note the alternative (or flexibility) as described
Table 1 Guidelines for Application of Tests All Dosage Forms	*Perform Biological Reactivity Tests, In Vivo <88> to obtain the appropriate Classification of Plastics Materials*	Class VI plastics are meant for use in implants. There is no reason to meet this requirement for inhalation or parenteral packaging materials of construction. The type of test should be specified. Tests other than USP tests should be allowed, e.g., ISO 10993. Since a material would not have a specific application for which the class could be determined, this would not be realistic; according to <1031> the component use is what determines which class of plastic is appropriate	Specify biocompatibility tests, e.g., tests for cytotoxicity, irritation and skin sensitization, systemic toxicity Biological reactivity tests should be performed on components not materials

<661.1> Section and/or Para	USP Text	Comment	Suggested Revision or Consideration for USP
Specifications	*Physiochemical*		Correct the spelling of "Physicochemical" throughout
Specifications	*Infrared bands*	LDPE - band at 1170 and 1375 is not typical Polypropylene - missing the major multiplet band in the range of 2950-2835 and a strong band near 1455	Remove 1170 and 1375 Add multiplet and 1455
Specifications	*Extractable Metals*	Specifications need not be placed on metals that are not generally of safety concern If there are elements expected these should be tested for and amounts reported; based on the application the pharmaceutical manufacturer will need to decide if the levels are safe The elements listed are not in line with the ICH Q3(D) draft. As example, germanium is not in the scope of ICH Q3(D) draft, and it is not clear why it should be tested. More importantly, however, is that the 'big four' elements (As, Hg, Pb, Cd) have not been included into the USP draft.	Change specification for metals that are not of general safety concern to "if expected, report result" Either a rationale for excluding As, Hg, Pb, Cd, should be provided, or a test for these four elements be included.
Specifications	*PET: Titanium: Solution S3 contains NMT 0.4 mg/L (ppm), corresponding to 0.1 µg/g.*	The acceptance criteria in the PharmEur is 1 ppm.	Please harmonize criteria
Specifications	*PVC: Acidity or alkalinity, extractable metals, additives*	There are different types of PVC, e.g. plasticized and non-plasticized resulting in different properties and specifications	Harmonize acceptance criteria with PharmEur, Consider incorporating all chapters for PVC from the PharmEur
Test methods - Identification - DSC	*For example, a DSC specification for a material that is not currently listed in this chapter should be consistent, in language and in rigor, with a DSC specification for a material*	This should be melt temperature -- melt index implies melt flow index which is quite a different test	Change "melt index" to "melt temperature"

<661.1> Section and/or Para	USP Text	Comment	Suggested Revision or Consideration for USP
	that is listed in this chapter (e.g., melt index agreement between sample and reference material)		
Test methods – Identification- Infared Spectrophotometry	*Refer to Spectrophotometry and Light-Scattering <851>.*		Reference IR specific chapter <1854> as well
Test methods – Identification- Infared Spectrophotometry Internal reflectance mode	*Before mounting the specimen on the plate, compress it to form a thin, uniform film by exposure to elevated temperatures under high pressure (2000 psi or more).* *Procedure: Place the mounted specimen sections in the sample compartment of the infrared…*	Please see USP <1854> for proper language - this should be ATR and film formation is not necessary or appropriate This procedure is not consistent with modern FTIR instrumentation and ATR accessories.	Remove instruction to prepare a thin film Change the instruction to: Place the sample on the ATR accessory so that it covers the crystal, apply adequate pressure via the mounting accessory to ensure good contact and collect enough scans to achieve appropriate signal intensity and resolution.
Test methods -- Thermal Analysis			A general instruction regarding the heating/cooling rates and ranges should be given, rather than detailed instruction. For example, rather than listing all the various conditions, the section could recommend using conditions where the standard provides the response specified and this should be the same for the sample.
Extractions	*Table 2 - S3*	The list of metals to be tested is not consistent with the specification list	Suggest pointing to specified metals in polymer specific sections
Plastic Additives - polyethylene, polyolefins,	*Reference solution B: 0.24 mg/mL of USP Plastic Additive 03 RS and 0.24 mg/mL of USP Plastic*	Both are additive 03	Please clarify this

<661.1> Section and/or Para	USP Text	Comment	Suggested Revision or Consideration for USP
polypropylene	*Additive 03 RS prepared in the Solvent mixture* *Reference solution P: 6.0 mg/mL of USP Plastic Additive 10 RS, and 6.0 mg/mL of USP Plastic Additive 10 RS prepared in methylene chloride.*	Both are additive 10	
Physicochemical Tests		These tests appear to be copied from the PharmEur, and while we appreciate this effort to harmonize, it is not clear what value these tests have. The tests seem to be unnecessary, and the information needed could be just as easily addressed by controlled extraction studies or supplier information. The chapters in PharmEur refer to specific drug products (mainly parenterals), they are not appropriate for all drug products including oral. Further, if a supplier provides certification that the material meets requirements and is the material is it claimed to be, then this should be sufficient.	We understand that materials need to meet specifications, but there may be ways that the materials can meet specifications other than by demonstrating that they meet all the proposed tests in this chapter. The extraction tests proposed do not provide more helpful information than what can be provided from suppliers/manufacturers (e.g., formulation sheets, and other testing results). Suggest adding the option to obtain confirmation of compliance by different methods than the testing methods outlined.
Plastic Additives		Several tests refer to TLC and visual comparison to a standard. Visual testing is difficult to calibrate and standardize and TLC is difficult to quantitate. Best addressed by routine extractable testing (HPLC or GC). Generally, the use of qualitative TLC methods are not preferred or appropriate, and there should be stated clearly the option to use validated, modern methods.	State clearly the option to use validated, modern methods such as HPLC or GC instead of or in addition to TLC.

<661.2> Plastic Packaging Systems for Pharmaceutical Use

<661.2> Section, item, and/or para	USP Text	Comment	Suggested Revision or Consideration for USP
Scope	*Plastic packaging systems for pharmaceutical use include bags, bottles, vials, cartridges, dry powder and metered-dose inhalers, nebulizers, prefillable syringes, blisters, pouches, and bottles or closures for capsules and tablets.*	Dry powder inhalers (DPIs) and metered dose inhalers (MDIs) typically include a combination of plastics, elastomers, foils, metal canisters, etc. Additionally, the terms dry powder inhaler and metered dose inhaler typically refer to the full drug product, i.e., to use USP terms – the packaging system and the pharmaceutical product. Further, it is arguable that the MDI container closure system and device (metering valve) taken together consists in substantial portion of non-plastic materials. Nebulizers are devices not packaging systems; specifically nebulizers are cleared via the 510(k) process in the US Consideration should be given to the current regulatory treatment of prefilled syringe products and whether these are to be treated only as packaging systems	Remove dry powder inhalers, metered dose inhalers and nebulizers and prefilled syringes from this list.
Scope	*A packaging system is chemically suited for its intended use with respect to safety if:* *The packaging system is constructed from well-characterized materials that have been intentionally chosen for use as established by testing according to Plastic Materials of Construction <661.1>.*	A packaging system is made of components according to the definition in USP <659>. The components may be intentionally chosen but the materials may not be in the purview of the pharmaceutical manufacturer to choose. The key is that the materials meet certain requirements. Requirements in <661.1> in practice will be applied by pharmaceutical manufacturers to primary packaging components, not materials of construction.	Suggest re-wording as follows: The packaging system is constructed from components that meet the requirements in Plastic Materials of Construction <661.1> or their safety has been demonstrated adequately.

<661.2> Section, item, and/or para	USP Text	Comment	Suggested Revision or Consideration for USP
Test Methods -- Biological reactivity	*In vitro biological tests are performed on the packaging systems according to the test procedures described in Biological Reactivity Tests, In Vitro 87*	It is unlikely that USP <87> could readily be performed on an entire packaging system. In cases where a packaging system contains elastomers, the test is to be conducted differently. This does not reflect Table 2 "Typical Suitability Considerations for Common Classes of Drug Products" of the FDA Guidance for Industry: Container Closure Systems for Packaging Human Drugs and Biologics, 1999, regarding safety, where reference to appropriate indirect food additive legislation is sufficient. Also the EMA guideline on plastic immediate packaging materials does not require more testing for oral drug products than for foodstuffs.	Please re-word, e.g., *In vitro biological tests are performed on the packaging systems or their components according to the test procedures described in Biological Reactivity Tests, In Vitro 87.* Further, such testing should not be required for Topical Delivery Systems, Topical Solutions and Suspensions, and Topical and Lingual Aerosols, Oral Solutions and Suspensions and Topical Powders, Oral Powders Oral Tablets and Oral (Hard and Soft Gelatin) Capsules
Test Methods -- Biological reactivity	*In addition, the in vivo testing described in Biological Reactivity Tests, In Vivo <88> is not required for packaging systems used with certain dosage forms (oral and topical products). Packaging systems that do not meet the requirements of the biological reactivity tests (<87> and <88>, if appropriate) are not suitable as packaging systems for pharmaceutical use.*	It is unclear what in vivo tests would be performed outside of selecting a Plastic Class based on USP <1031>. Class VI plastics are meant for use in implants. There is no reason to meet this requirement for inhalation or parenterals. The type of test should be specified. Tests other than USP tests should be allowed, e.g., ISO 10993.	Please clarify with respect to need for performing in vivo tests outside of selecting a Plastic Class based on USP <1031>. Specify biocompatibility tests, e.g., tests for cytotoxicity, irritation and skin sensitization, systemic toxicity
Physicochemical tests	*Physiochemical Tests*	The use of a water extraction is not relevant for an MDI or solid dosage form system. A risk based approach should be taken, which is appropriate to processes and product. For example, if a packaging system is known to contain particular additives and product is high	Correct the spelling of "Physicochemical" Risk-based language should be included that incorporates concepts noted in the comment column, e.g., a risk-based approach should be taken, which is appropriate to processes and product. For example, if a packaging system is

<661.2> Section, item, and/or para	USP Text	Comment	Suggested Revision or Consideration for USP
		risk then extraction studies will be completed, and the listed physicochemical tests are not necessary (i.e., they will not add further useful information). If a particular conversion process is known to introduce additives in addition to those in the material, then these should be targeted in extraction studies	known to contain particular additives and product is high risk then extraction studies will be completed, and the listed physicochemical tests are not necessary (i.e., they will not add further useful information). If a particular conversion process is known to introduce additives in addition to those in the material, then these should be targeted in extraction studies. Provision should be made for testing components.
Chemical Safety Assessment	*With regard to the testing of the packaging system and the packaged drug product, an appropriate and rigorous chemical safety assessment would include extractables testing of the packaging system and leachables testing of the packaged drug product.*	This does not reflect Table 2 "Typical Suitability Considerations for Common Classes of Drug Products" of the FDA Guidance for Industry: Container Closure Systems for Packaging Human Drugs and Biologics, 1999, regarding safety, where reference to appropriate indirect food additive legislation is sufficient. Also the EMA guideline on plastic immediate packaging materials does not require more testing for oral drug products than for foodstuffs.	Remove testing requirement for low risk products and refer to indirect food contact legislation