IPAC-RS

International Pharmaceutical Aerosol Consortium on Regulation & Science

1500 K Street NW • Washington DC • 20005
Telephone +1 202 230 5607 • Fax +1 202 842 8465
Email info@ipacrs.org • Web www.ipacrs.org

November 1, 2023

IPAC-RS Comments on "USP <429> "PARTICLE SIZE ANALYSIS BY LASER LIGHT DIFFRACTION**" [PF 49(5)]**

Submitted by email to: Edmond Biba, Senior Scientific Liaison for USP General Chapters, exb@usp.org

IPAC-RS is an international association of companies that develop or manufacture orally inhaled or intranasal drug products, such as metered dose inhalers, dry powder inhalers, and nasal sprays. Current IPAC-RS members and associate members are listed at About | IPAC-RS (ipacrs.org)

The mission of IPAC-RS is to advance scientifically driven approaches to enhancing product quality of inhaled and intranasal drug products for the benefit of patients. As such, IPAC-RS commends USP for preparing chapter <429> and providing it for public comment.

IPAC-RS members have carefully reviewed the chapter and prepared the following comments for your consideration.

Line by Line Comments referring to the pdf of 7 pages total (as downloaded from USP–NF/PF (uspnf.com))

Location	Original Language	Proposed Changed Language	Justification of Proposed Change	Type
Page 1, Preface (above Introduction)	The method is based on the ISO standards 13320-1(1999) and 9276-1/AC1 (2004).	The method is based on the ISO standards 13320:2020 and 9276-1/AC1 (2004).	Any new or revised USP chapter that is based on an ISO document should be based on the current version of that document. Of course, the statement must actually be true.	Critical
Page 2, Principal, 1st sentence	A representative sample, dispersed at an adequate concentration in a suitable liquid or gas, is passed through a beam of monochromatic light, usually a laser.	A beam of monochromatic light (usually a laser) is passed through a representative sample, dispersed at an adequate concentration in a suitable liquid or gas.	Original language ignores the need to measure non-aerosolized particles (e.g., particles in liquids) as might be done for incoming raw materials.	Critical
Page 2, Principal, 4th sentence	These scattering pattern values are then transformed, using an appropriate optical model and mathematical procedure to yield …	These scattering pattern values are fitted to an appropriate optical model to yield, …	Simplify language	Minor
Page 2, Instrument, 1st sentence	The instrument is located in an environment where it is not affected by electrical noise. Mechanical vibrations, temperature fluctuations, humidity, or direct bright light.	The instrument is located in an environment where it is not affected by electrical noise. Mechanical vibrations, temperature or humidity fluctuations, or direct bright light.	Simplify and correct language (humidify can also fluctuate).	Regular
Page 3, Instrument, 5th paragraph	These lenses create a scattering pattern that, within limits, does not depend on the location of the particles in the light beam.	These lenses modify the scattering pattern such that, within limits, it does not depend on the location of the particles in the light beam but only upon their size.	Correct language (the lenses don't **create** the scattering pattern).	Regular

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Page 4, Operation of the Liquid Dispersion. Insert ahead of last paragraph		Use of a recirculating system must not alter the size of the test material.	Correct for missing caution	Critical
Page 4, Determination of the Concentration Range, 2nd paragraph	In view of the above, measurements must be performed at different particle concentrations to determine the appropriate concentration range for any typical sample of material.	In view of the above, measurements must be performed at different particle concentrations to determine the appropriate concentration range for a typical sample of the target material.	Simplify and clarify language	Minor
Page 5, Validation, last sentence	The change of the dispersing energy may be monitored by the change in the particle-size distribution.	The effect of the dispersing energy may be monitored by the change in the particle-size distribution.	It is the effect of the dispersing energy that is of interest	Regular
Page 5, Measurements Precautions, 2nd sentence	Efforts are made to reduce contributions from these sources.	Efforts must be made to reduce contributions from these sources.	Better to be prescriptive in this case. (note that the author uses “must” a few sentences below).	Regular
Page 5, Measurements Precautions, 2nd bullet point	Earth all instrument components to prevent ignition of solvents or dust explosions;	Ground all instrument components to prevent ignition of solvents or dust explosions;	In the US we typically use the word “ground”.	Minor

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Page 5, Measurements Precautions, last sentence	In the case of wet dispersions, avoid air bubbles, evaporation of liquid, schlieren or other inhomogeneity in the dispersion; similarly, avoid improper mass-flow from the disperser or turbulent airflow in the case of dry dispersions; such effects can cause erroneous particle-size distributions.	What does “improper mass-flow” mean	Clarification is needed.	Regular
Page 5, Measurements, Measurement of the Light Scattering of Dispersed Sample(s)	The coordinates (size and position) of the detector elements together with the focal distance of the lens determine the range of scattering angles for each element.	The coordinates (size and position) of the detector elements together with the focal distance of the lens determine the range of scattering angles imaged (or seen, or observed) by each element.”	Clarify the language	Minor

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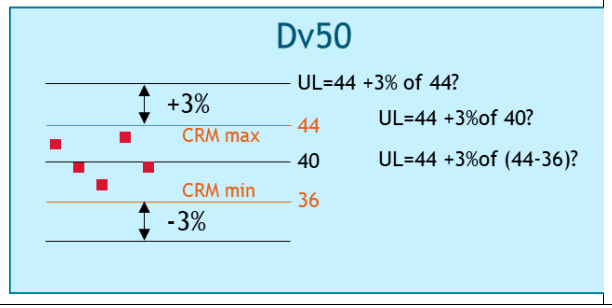
Page 6, Instrument Qualification, Operation Qualification, 4th sentence	This can be undertaken using any certified reference material (CRM) that is acceptable in industrial practice, which is characterized by a metrologically valid procedure for one or more specified properties, accompanied by a certificate that provides the value of the specified property, its associated uncertainty (ucRM) and a statement of metrological traceability.	This can be undertaken using any certified reference material (CRM) that is acceptable in industrial practice, characterized by a metrologically valid procedure for one or more specified properties, and accompanied by a certificate that provides the value of the specified property, its associated uncertainty (ucRM) and a statement of metrological traceability.	Simplify language	Minor
Page 6, Instrument Qualification, Operation Qualification, 8th sentence.	They shall have a known distribution over an appropriate size range such that, for example. The x_{90}/Jx_{10} ratio Is at least 1.5.	They will have a known distribution over an appropriate size range such that, for example. The x90/Jx10 ratio Is at least 1.5.	CRMs are carefully characterized, well understood materials that **will** have certain specified properties.	Regular
Page 6, bottom, Operation Qualification	…independent measurements does not deviate by more than 3%....	Clarify - 3% of what?: For example, of the value of the limits? Of the range between limits? Of the average o?	Consider adding a graphic to avoid mis-interpretation. For example: 	Regular