Defining the dosage strength for labeling of DPIs: Use, limitations and relevance of *in vitro* data

Uniformity of delivered dose testing and labeling: An overview

Jagdeep Shur, PhD[a]; Robert Price, PhD[a]; Tim Rouse, BSc[b]; David Lewis, PhD[b]; Dilraj Singh, PhD[c]; Bradley Morrical, PhD[c] and Stephen Edge, PhD[c]
[a]University of Bath
[b]Chiesi, Ltd.
[c]Novartis Pharma AG

Introduction

Marketed dry powder inhaler (DPI) products utilize various formulation and device technologies to achieve consistent delivery of the efficacious dose of active pharmaceutical ingredient(s) (APIs) to the patient. However, regardless of the drug delivery platform, this dose must be of an appropriate quality and aerodynamic particle size distribution (APSD) to deposit in the target region of the lung and achieve the desired therapeutic effect.[1] The general and simplistic concept that the APSD of the API must be < 5 µm in order to reach the deep lung is a useful guide for the development and quality control of both innovator and generic inhaled products. But it can be asked how this descriptor and concept relate to any established labeled dose or strength of an inhaled product, such as a DPI, and which methods were used for that determination.

The terms used to describe the dose of DPI products appear in several pharmacopoeial tests for DPIs. For example, the European Pharmacopoeia (Ph. Eur.) not only describes methodologies to be used to determine the APSD and the metric fine particle dose (FPD), but also contains a test for the assessment of the uniformity of delivered dose (UDD), with acceptance limits. In contrast, even though the United States Pharmacopoeia (USP) describes a delivered dose uniformity test, albeit with no prescribed limits, it has, in contrast to Ph. Eur., no description of any APSD metric such as fine particle dose.[2] (Not all regions or countries' guidances/pharmacopoeias use the wording "uniformity of delivered dose" to represent the delivered dose test, but this phrase will be used throughout this article). Clearly, such descriptions and disparities in pharmaceutical tests that use the word "dose" within regulatory source documents may be somewhat confusing.

The development of inhaled products: Defining the dose

During early phase pharmaceutical development, where the optimal efficacious dose or dosing regimen has not yet been defined, technical and clinical drug product batches (including different strengths) are used to elaborate the *in vitro* specifications for the DPI product, including the APSD and UDD. However, in contrast to the APSD test, through all the stages of clinical development, the DPI product must comply with the applicable pharmacopoeial/regulatory prescribed limits of a test for UDD, unless both justified and authorized by competent authorities. The specifications for any APSD metrics and delivered dose of the product are only finalized after the health authority's review and approval of the marketing authorization dossier.

Again, the key question regarding these two important critical quality attributes is which is more relevant for describing the dose, and thereby the efficacy, of the product, and which is therefore more appropriate for the labeling of an inhaled product such as a DPI. Indeed, it may appear somewhat surprising that, despite not being related to any APSD metric, limits for UDD are prescribed across several regulatory sources, whereas there are no limits/criteria for any more clinically relevant APSD metrics, except in the Chinese Pharmacopoeia (ChP), which has a somewhat arbitrary fine particle frac-

tion limit of ≥ 10% for DPIs.[3] An additional, potential area of confusion for understanding the dose of DPIs is that phrases such as "metered," "pre-metered," "pre-dispensed" and "device-metered" are used in regulatory documents and product information literature.

The dose conundrum for inhaled products and product labeling

As with standard solid dosage forms, commercial DPIs are typically labeled with a label claim, which, in simple terms, is essentially the strength or dose of the product. For DPIs, however, the understanding of dose is more complex than for standard solid dosage forms because the entire labeled dose never reaches the target region of the patient's lung; and a medical device plays a pivotal role in the delivery of the API into the body. It is important to remember that label claim, labeling and label can also have subtly different definitions, and therefore interpretations. For example, USP<7> defines labeling as "all labels and other written, printed, or graphic matter on an article's immediate container, or in, any package or wrapper which it is enclosed," and label as "that part of the labeling on the immediate container."[4]

The label claim/labeling of DPIs

Some examples of the current source documents for definitions and requirements for the label claim and labeling of DPIs are presented in Table 1. There are some similarities and differences in the ways the US and European regions describe the label claim/labeling aspects of DPIs. For example, both the US and European source documents describe the use of the active moiety, with the US preferring this as the metered dose and Europe, the delivered dose. However, there have also been various changes in the ways some regional source documents consider labeling. For example, in Europe, the Ph. Eur. 0671 proposed a more specific text for labeling in 2018, changing from "the delivered dose; alternatively, where the dose has been established as a metered dose or as a pre-dispensed dose, the label states either the metered dose or the pre-dispensed dose, as appropriate" to "the delivered dose or, if justified and authorised (e.g., where the dose has been established as a metered dose or as a pre-metered dose), the metered dose or pre-metered dose."

This change in approach, however subtle, suggests that the delivered dose is becoming the preferred term for the label claim/labeling of inhaled products for the Ph. Eur. Interestingly, the corresponding European Medicines Agency (EMA) inhaled product quality guideline defines the label claim as "the amount of drug (usually on a per actuation basis) declared on the label of the product" and indicates that inhaled products should be labeled with the delivered dose.[1] Conversely, the 2018 FDA draft guidance, in alignment with the FDA definition of strength, clearly states that the "labeling of oral DPIs should state the established name of the product as (Drug) Inhalation Powder and provide the strength

Table 1

Labeling definitions and requirements for dry powder inhalers (DPIs), as described in source documents from the United States Pharmacopeia (USP), European Pharmacopeia (Ph. Eur.), European Medicines Agency (EMA) and the United States Food and Drug Administration (FDA)

Source Document	Labeling and Label Claim for Dry Powder Inhalers (DPIs)
Ph. Eur.	Ph. Eur. 0671. Labeling: The delivered dose or, if justified and authorized (e.g., where the dose has been established as a metered dose or as a pre-metered dose), the metered dose or pre-metered dose.[6]
EMA Guideline	Label claim: The amount of drug (usually on a per actuation basis) declared on the label of the product. Labeling (SmPC): The content per actuation can be expressed either as ex-valve (metered dose) or ex-actuator (delivered dose). All products containing NCEs and products containing known drug substances used in inhalation for the first time should be labeled with the delivered dose or an appropriate alternative (e.g., fine particle mass) where agreed with the regulatory authorities.[1]
EMA Standard Terms	In Europe, standard terms for DPIs are: inhalation powder; inhalation powder, hard capsule; inhalation powder, pre-dispensed; inhalation powder, tablet.[12]
USP<5>	Inhalation and nasal drug products—general information and product quality tests. The established name for a DPI is inhalation powder.[13]
USP<7>	Labeling. Labels and labeling of drug products shall be expressed as active moiety in name and strength.[4]
FDA Draft Guidance, 2018	DPIs: Labeling: (Drug) Inhalation powder and provide the strength as the amount per metered dose unit. Prescribing information: The metered amount of medication to be delivered to the patient.[5]

Definitions: SmPC = Summary of product characteristics; NCE = New chemical entity

as the amount per metered dose unit" and "the metered amount of the drug from a DPI is used to denote its strength, not the specified target delivered dose."[5] However, in contrast to the EMA quality guideline, the inhalation-relevant chapters in the USP and Ph. Eur. and the 2018 FDA draft guidance do not have a specific definition of label claim, and only the USP suggests that the label claim is usually the pre-metered or metered dose of the drug. Such different approaches make the development of any unified concept of label claim challenging, not only from a labeling perspective, but also, importantly, for the understanding of the dose of DPIs.

While it does seem clear that the metered dose or the delivered dose is to be used in the label claim/labeling of DPIs, it is interesting to note that the EMA quality guideline does state that the labeling can be an alternative to the delivered dose, and gives the example of fine particle mass.[1] Even so, the overwhelming majority of marketed DPIs are labeled based on the metered or delivered dose. Generally, at least in Europe, it appears that the expectation for label claim/labeling of DPIs is that of delivered dose. In contrast, in the US, the 2018 US draft guidance states that for DPIs, the labeling should contain the amount per metered dose unit with additional information, such as the target delivered dose, with corresponding specified *in vitro* test conditions, to be contained in the prescribing information of the product.[5]

The consequences of regional labeling requirements for DPIs

The practical consequence of different regional approaches for the label claim and labeling of DPI products is that products having identical compositions may have different label claims (numerical strength/dose on the device/packaging). This potential confusion is further compounded since compositionally identical products may have different regional trade/brand names or brand color schemes.

A good example is the pre-dispensed, dual blister strip DPI combination product from GSK named Relvar® Ellipta® in Europe and Breo™ Ellipta™ in the US, which contains two APIs, namely flucticasone furoate and vilanterol trifenatate. From the publically available product information documentation, the loaded (pre-dispensed) dose of each API is the same in both the European and US versions of the product. However, in terms of the numerical strength/dose on the device label, the US product uses the metered (pre-dispensed) dose, expressed in terms of API moiety, as the product label claim/strength (100/25 µg for fluticasone furoate and vilanterol, respectively), whereas in Europe, the delivered dose of the API moiety is used for the product label claim/strength (92/22 µg for fluticasone furoate and vilanterol, respectively). Even though the clinical efficacy of both products would be expected to be the same, the differing dose/strength labels between these two regional products could easily cause them to be perceived as products of different strengths. This would not be expected to impact prescribers or patients since such differently labeled products are not available inter-regionally. However, such apparent differences would need to be considered in some aspects of development, such as comparator studies or the design of clinical trials.

One could also ask whether the inclusion of any APSD metric in the labeling of DPIs would not create further confusion because there would then be dose values for the metered dose, delivered dose and any APSD metric, especially if older approved products were updated. It is clear that the delivered dose is an integral part of the testing and labeling of DPIs, but the nature of the numerical value relative to the delivered dose needs to be considered.

Uniformity of delivered dose testing: Practicalities and limitations

Analytical results generated during release and stability testing may often be reported as mean values and will exhibit a degree of variability. The same is true for the UDD test. Currently, the UDD test is typically performed with zero tolerance acceptance criteria (a counting test), although the test may be moving towards a parametric tolerance interval test (PTIT).[5] There are two principal facets of the delivered dose result generated by the current UDD test, namely the number of individual results generated to calculate the mean (which is the actual delivered dose) and the limits/requirements of the test.

The actual delivered dose is the mean of a set of data and, in terms of the final commercial product, the label claim (or target) delivered dose will be the value determined as representative of the final product. The USP states that "its value reflects the expected mean drug content for a large number of delivered doses collected from the product using the method specified in the monograph."[2] The determined mean delivered dose is evaluated against the established label claim/target delivered dose in Ph. Eur.,[6] Japanese Pharmacopoeia (JP),[7] EMA quality guidelines[1] and the 2018 FDA draft guidance,[5] with limits of 85-115%. This single value mean result will not, however, represent any variability of the underlying individual values used to calculate the mean nor the specific batch being tested (as it would be using PTIT).

There are two aspects to understanding the potential number of UDD individual results/actuations, to be used to calculate the delivered dose, namely the prescribed number of individual results including so-called level 1 (first tier) and level 2 (second tier) testing, and whether inter/intra-device testing is required.

The number of individual results for the UDD counting test

The regional regulatory limits for the individual results in the UDD test are well known and will not

be elaborated here. All of the regulatory source documents have zero tolerance acceptance criteria based on the mean result[3,6,7] or the label claim.[5,7] It appears that there is a general global consensus and harmonization for the number of results to be generated in the UDD test, with the mean value being generally generated from 10 results (USP and 2018 FDA draft guidance, 20 for device-metered DPIs) for level 1 testing; if level 1 testing limits are not met and further testing is permitted based on level 1 results, a total of 30 results (2018 FDA draft guidance, 60 for device-metered DPIs), if level 2 testing limits are met. Therefore, the result reported for the delivered dose may be based on up to 60 individual results. This value may be higher if PTIT is used, as proposed in the 2018 FDA draft guidance.

There are no limits/requirements for the UDD test in the USP and, instead, reference is made to the individual product monograph. The only requirements for the limits of a UDD zero tolerance test in the US appear in the 2018 (and 1998) FDA draft guidance, which describes level 1 and level 2 testing based on the label claim, albeit with different (tighter) criteria than the Ph. Eur/JP/ChP. It is also not clear how USP<601> and the 2018 FDA draft guidance are aligned for level 2 UDD testing. Additionally, the 2018 FDA draft guidance states that the mean of the initial and last of the label claim doses should be evaluated separately, and it is unclear how this relates to the development of the target delivered dose.

Regardless whether the delivered dose is evaluated based on the average result or the label claim, the range of the limits in the various source documents may appear somewhat broad, especially when considering this test is used to generate the label claim and/or labeling of the DPI product. This potential variability of UDD results is further exemplified as the Ph. Eur. and JP allow the limits of the UDD test to be extended to ± 50%, if justified and authorized.

Intra/inter-device testing of UDD of DPIs

It is important to consider that some of the variability in the UDD results will be associated with any inter/intra-device variability. The importance of inter/intra-device variability in any evaluation of the delivered dose of DPIs, and the way this should be formally evaluated, is being increasingly recognized in the various regional regulatory source documents. It can be seen from Table 2 that for multi-dose DPIs, intra-device and inter-device variability should be assessed during the development of DPIs, either in a combined intra/inter-device test or as two separate tests. However, the situation is not harmonized across the regulatory pharmacopoeia/guidance sources. For pre-metered systems, such as those based on single-dose blister or capsule products, it is not completely clear if the products should be tested based on 1 device/1 capsule (inter-device) or 1 device/10 capsules (intra-device); only the Ph. Eur. indirectly suggests the latter situation in the wording for level 2 testing.

Several regulatory source documents now provide information about the ways such inter-device testing may be performed for multi-dose inhalers. For example, in 2018, the Ph. Eur. included an outline for a testing regimen in the Production (non-release) section of Chapter 0671 that involves the collection of a single dose from each of 10 inhalers, collecting the dose at the beginning (from 3 inhalers), middle (from 4 inhalers) and end (from 3 inhalers).[6] Since there are no limits for such inter-device testing for DPIs in Ph. Eur., the actual purpose of such a Production test description is questionable, especially when considering the evolution of the delivered dose label claim. Clearly, if this were in the Tests (release) section, a considerable increase in testing would be formally required for multi-dose DPIs. In the US, the 2018 FDA draft guidance harmonizes with the USP, both of which now prescribe testing a dose at the beginning and end of the labeled number of doses of 10 multi-dose devices, which essentially represents a simple combined intra/inter-device test. Indeed, the 2018 FDA draft guidance suggests that APSD should also be determined at the start and end doses of multi-dose DPIs. The JP and ChP follow a similar approach to that of the US for UDD testing of multi-dose products, in that essentially 10 doses are collected from 10 devices. However, compared to the US, the doses are collected only from the beginning of the device labeled doses, and not additionally at the end.

Even though there is, from a quality perspective, a clear need to evaluate inter-device variability, there is already an apparent difference in approaches for how and when this should be evaluated, as shown by the example above with the ChP and USP (release test) and Ph. Eur. (non-release test). The possibility of having a single test for both intra- and inter-device variability in Europe is also exemplified by the fact that the EMA is considering a proposal to include such a combined test in any updated EMA quality guideline for the specification of the final drug product.[8] Nevertheless, the development of such an all-encompassing test would not be without challenges.

It is clear that intra-device testing and inter-device testing of multi-dose DPIs requires a considerable number of device actuations and is not without some further effort by the sponsor. This is exemplified by the pharmacopoeial inter-device testing of a product such as Bricanyl® Turbuhaler® (terbutaline sulfate, AstraZeneca) 250 microgram, which contains 200 labeled doses per inhaler. The number of actuations required for such a multi-dose DPI product could be up to more than 1,000, merely for level 1 testing if Ph. Eur. or USP was followed, even though only 10 or 20 actuations/doses would be col-

lected and analyzed for Ph. Eur. and USP, respectively. Conversely, only 10 actuations and analyses would be required if ChP and JP was used as the source regulatory testing document.

It can be envisaged that, for Ph. Eur. and USP, the number of actuations (and devices) would be significantly multiplied should level 2 testing be required, suggesting that for multi-dose devices which contain more than 100 doses, several thousand actuations of the devices may be required to comply with any requirements for UDD. Moreover, only the ChP, JP and 2018 FDA draft guidance provide an indication of the limits to be used for the evaluation of the individual values generated during inter-device testing and any level 2 testing (an additional 20 devices). Importantly, only the JP and 2018 FDA draft guidance have any limits for the mean delivered dose, in that the mean values determined during inter-device delivered dose testing must be within ± 15% of the label claim for delivered dose.

Other aspects of the delivered dose

There is one important aspect of the delivered dose and its relationship to the APSD, the so-called mass balance. This evaluation requires that the mass of API emitted during the cascade impactor determination of APSD is assessed against either the delivered dose from the UDD test, with limits of ± 25% of the mean delivered dose applying in Ph. Eur., and JP, or ± 15% of the target delivered dose in USP and the 2018 FDA draft guidance. This is an important point because this evaluation essentially inextricably links the emitted dose from the APSD test to the delivered dose in the UDD test. It could be argued that the determination of the emitted dose during the APSD testing is also a measure of the delivered dose, albeit, an indirect one. In terms of its relevance to the efficacious dose, the UDD can be presently considered as essentially a quality control test, which through the mass balance evaluation provides a system suitability test for the APSD test.

The delivered dose is also an important parameter used in additional development pharmaceutics/characterization studies (for example, the effect of flow rate, product robustness, etc.) as well as for the development of generic DPIs. In Europe, the EMA guidelines on the requirement for clinical documentation of orally inhaled products states that the target delivered dose of the generic product should be similar to the reference product (within ± 15%).[9] This is in general agreement with the Ph. Eur. and EMA guidelines for the delivered dose, which require that the mean delivered dose determined during the UDD test must be within 15% of the label claim.

In contrast, the 2018 FDA guidance for generic products based on, for example, fluticasone propionate and salmeterol xinafoate, do not provide any limits for the evaluation criteria for the delivered dose of the test and reference products, but simply state that the single actuation content should be

Table 2

Uniformity of delivered dose intra/inter-device testing parameters for multi-dose dry powder inhalers 2018

(S = start, M = middle, E = end)

	Device-Metered, Multi-Dose Dry Powder Inhaler (DPI) Testing Parameters			
	Intra-Device	Level 2 Testing	Inter-Device	Level 2 Testing
FDA Draft Guidance 2018	10 devices 1S/1E[1]	20 additional units	-[1]	-[1]
USP<601>, 2018[2]	10 devices 1S/1E	No	-[1]	-[1]
EMA Guideline, 2006	Adapt to test intra- and inter-device variability	No	-	-
Ph. Eur. 0671, 2018	3S/4M/3E	Additional 2 inhalers	10 inhalers 3S/4M/3E	No
JP XVII, Supplement I, 2018	3S/4M/3E	Additional 2 inhalers	10 inhalers 10S	Additional 20 inhalers
ChP 0111, 2015 (Eng)	3S/4M/3E	Additional 2 containers	10 devices 10S	Additional 20 containers

[1] This is not defined as an intra- or inter-device test, but the testing does encompass inter- and intra-device testing.

[2] USP<601> states that the test for Delivered Dose Uniformity over the entire unit life is required. This test is also an indirect test of inter-device variability.

determined; the guidance also provides advice for population bioequivalence on an evaluation of the single actuation content.[10] While for those with some knowledge of the art, this reverse engineering matching of delivered doses may appear to be not insurmountable, a thorough understanding of the delivered dose practicalities is required for the assessment of the delivered dose during the shelf-life of any test and reference products. This is especially true when considering the EMA guidelines for the *in vitro* equivalence of impactor stage groupings between reference and test products, which states that a difference of ± 15%, for example, may be justifiable.

It should be noted that this often-stated limit of ± 15% is only an example, perhaps recognizing potential variability with different inhaled products. It is presumed that any comparison would be valid through the shelf-life of the test product. While the delivered dose would be fixed at ± 15% of the (target) label claim of the reference product, it would also be linked to the APSD by the previously mentioned mass balance evaluation. It could be argued that stability/shelf-life data is generally not publically available, and any stability studies performed for the test (and reference) products would be subject to parameters such as the age of the reference product. Consequently, confirmation of any such comparison limits for delivered dose and stage groupings could only be confirmed during long-term stability studies. It may also be that wider APSD (and delivered dose) limits than ± 15% may be justifiable, as for some commercial products this limit may be accepted as being not practicable.

For example, the commercial product Seebri® Breezhaler® (glycopyrronium bromide, Novartis) is controlled to ± 25% of its mean FPM (20-33 µg) (< 5 µm), based on the label claim of 50 µg of the premetered dose of the API moiety, glycopyrronium.[11] Moreover, such wide ranges in any APSD metric, such as the previously mentioned FPM, may impact the UDD, especially if the ± 15% limits are adhered to, posing obvious development challenges. However, any publically available information on delivered dose and any APSD metrics would certainly support the development of generic products and their consideration by health authorities.

Conclusions

The delivered dose is an important quality characteristic for the development and quality control of innovator and generic DPIs. However, in contrast to the more clinically relevant APSD test, the UDD test alone provides no indication of any APSD characteristic of a DPI. Importantly, the delivered dose and APSD tests are inextricably linked by the mass balance assessment. Therefore, even though the number of actuations for the two tests may be different, the value of such a UDD test for DPIs could be questioned when a similar parameter is available from the APSD test. Although the use of delivered dose serves as a nominal amount of drug delivered to the patient when labeling DPIs, careful consideration should be given to the fact that this dose expression is not representative of the amount of drug deposition in the lungs and to the analytical methodologies and practicalities of such tests. Labeling the dose of DPIs relative to an APSD metric, as included as a labeling option within the EMA quality guideline, would provide a more clinically relevant definition of dosage strength.

It appears that regulators do not typically require that such APSD metrics are included in any publically available product information and industry does not seem to proactively disclose this. Indeed, even though some APSD stage grouping limits for some products are available in the USP, the general lack of publically available originator DPI APSD specifications is a major challenge for the development of generic DPIs. If any such APSD metrics were required to be included in any label claim/labeling, then this would need the consensus of the various regional regulatory bodies such as the FDA, EMA, etc. and industry groups such as the International Pharmaceutical Aerosol Consortium on Regulation and Science (IPAC-RS), the European Pharmaceutical Aerosol Group (EPAG) and others. Until that time, it appears that the delivered dose will continue to be an important metric for the label claim/labeling of DPIs and, as such, a full understanding of this metric is required.

References

1. European Medicines Agency Committee for Medicinal Products for Human Use (CHMP). Guideline on the pharmaceutical quality of inhalation and nasal products. EMEA/CHMP/QWP/49313/2005 Corr. 2006. Issued June 21, 2006. Available at: http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2009/09/WC500003568.pdf.

2. United States Pharmacopoeia 41. 2018. Inhalation and nasal drug products: aerosols, sprays, and powders—performance quality tests <601>.

3. Chinese Pharmacopoeia (English version). 2015. 0111 Preparations for inhalation.

4. United States Pharmacopoeia 41. 2018. Labeling <7>.

5. FDA Center for Drug Evaluation and Research (CDER). Metered dose inhaler (MDI) and dry powder inhaler (DPI) products - quality considerations guidance for industry (draft). Revision 1. Issued April 2018. Available at: https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM070573.pdf.

6. European Pharmacopoeia 9.5. 2018. Preparations for inhalation 0671 Inhalanda.

7. Japanese Pharmacopoeia XVII, Supplement I. 2018. 6.14 Uniformity of delivered dose for inhalations.

8. Vincenzi, C., 2017. Update on the guideline on the pharmaceutical quality of inhalation and nasal products. Drug Delivery to the Lungs 2017.

9. European Medicines Agency Committee for Medicinal Products for Human Use (CHMP). Guideline on the requirement for clinical documentation for orally inhaled products. 2009. CPMP/EWP/4151/00 Rev. 1. Available at: http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2009/09/WC500003504.pdf.

10. FDA Draft guidance on fluticasone propionate; salmeterol xinofoate. 2013. Available at: http://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm367643.pdf.

11. Therapeutic Goods Administration ADoHaA: Australian Public Assessment Report for glycopyrronium (as bromide). 2013. Available at: https://www.tga.gov.au/sites/default/files/auspar-glycopyrronium-130710.pdf.

12. EDQM Standard Terms Database. http://standardterms.edqm.eu. Reproduced with the permission of the European Directorate for the Quality of Medicines & HealthCare, Council of Europe (EDQM). Retrieved on September 5, 2018. The EDQM Standard Terms database is not a static list and content can change over time.

13. United States Pharmacopoeia 41. 2018. Inhalation and nasal drug products—general information and product quality tests <5>.

Jagdeep Shur, PhD is a Research Fellow and Robert Price, PhD is a Professor at the University of Bath, www.bath.ac.uk. Tim Rouse, BSc is a Senior Scientist and David Lewis, PhD is Director of Aerosol Research at Chiesi, Ltd., www.chiesi.com. Dilraj Singh, PhD is a Director of Global Regulatory Affairs CMC, Bradley Morrical, PhD is an Analytical Network Leader and Stephen Edge, PhD is an Analytical Expert at Novartis Pharma AG, www.novartis.com. Corresponding author: David Lewis, PhD, Chiesi, Ltd., Units T1 - T3, Bath Road Industrial Estate, Chippenham, Wiltshire, SN14 0AB, Tel.: +44 1249 466930, d.lewis@chiesi.com.