



February 15, 2008

#### PDA Global Headquarters

Bethesda Towers  
4350 East West Highway  
Suite 200  
Bethesda, MD 20814 USA  
Tel: +1 (301) 656-5900  
Fax: +1 (301) 986-0296  
www.pda.org

#### OFFICERS

Chair:  
**John Shabushnig, PhD**  
Pfizer Inc  
Chair-Elect:  
**Maik Jornitz**  
Sartorius Stedim Biotech  
Secretary:  
**Rebecca Devine, PhD**  
Regulatory Consultant  
Treasurer:  
**Anders Vinther, PhD**  
Genentech, Inc.  
Immediate Past Chair:  
**Vincent Anicetti**  
Genentech, Inc.  
President:  
**Robert Myers**

#### DIRECTORS

**Harold Baseman**  
ValSource LLC  
**Véronique Davoust, PhD**  
Pfizer Inc  
**Lothar Hartmann, PhD**  
Hoffmann-La Roche  
**Yoshihito Hashimoto**  
Chiyoda Corporation  
**Louise Johnson**  
Aptuit  
**Stefan Köhler**  
AstraZeneca  
**Steven Mendivil**  
Amgen  
**Michael Sadowski**  
Baxter Healthcare Corporation  
**Amy Scott-Billman**  
GlaxoSmithKline  
**Gail Sofer**  
GE Healthcare  
**Laura Thoma, PharmD**  
University of Tennessee  
**Martin Van Trieste**  
Amgen, Inc.  
General Counsel:  
**Jerome Schaefer, Esq.**  
O'Brien, Butler, McConihe &  
Schaefer, P.L.L.C.  
Editor, *PDA Journal of  
Pharmaceutical Science  
and Technology*:  
**Lee Kirsch, PhD**  
University of Iowa

Division of Dockets Management (HFA-305)  
Food and Drug Administration  
5630 Fishers Lane, rm. 1061  
Rockville, MD 20852

- **Reference: International Conference on Harmonisation ; Draft Guidance on Q4B Evaluation and Recommendation of Pharmacopoeial Texts for Use in the ICH Regions; Annex 3 on Test for Particulate Contamination: Subvisible Particles General Chapter; Docket No. 2007D-0459**

Dear Sir/ Madam,

The Parenteral Drug Association (PDA) is pleased to offer comments on the draft guidance *Q4B Evaluation and Recommendation of Pharmacopoeial Texts for Use in the ICH Regions; Annex 3: Test for Particulate Contamination: Subvisible Particles General Chapter*, as published in the Federal Register on December 17, 2007. PDA is a non-profit international professional association of more than 10,000 individual member scientists having an interest in the fields of pharmaceutical, biological and device manufacturing and quality. Our comments which are attached in the accompanying table were prepared and reviewed by a team from our Regulatory and Quality Committee (RAQC), representing a global cross section of PDA members

PDA has been monitoring the progress of the ICH Q4B Expert Working Group and would like to express our support of their efforts, in conjunction with the Pharmacopoeial Discussion Group, to develop harmonized procedures for common compendial methodologies. This collaborative effort has resulted in the posting of this and other Annexes that will benefit global pharmaceutical manufacturers by expediting approvals and filing revisions worldwide. Global manufacturers have long struggled with trying to determine the most appropriate compendial method to register for their products. There have traditionally been variations between compendial methods measuring the same product/component characteristic or attribute. In some instances these methodology differences required the industry to perform unnecessary and redundant tests to satisfy regulatory expectations in a specific geographical region. The work of the ICH to alleviate this incongruity is commendable.

Please feel free to contact me if there are any questions or we can assist in these efforts.

Sincerely,

**Robert B. Myers**  
President, PDA

Enc: PDA Comment Table

## PDA Comments on Draft Guidance Q4B Evaluation and Recommendation of Pharmacopoeial Texts For Use in the ICH Regions; Annex 3: Test for Particulate Contamination: Sub-Visible Particles

### General Comments

- Text additions are in **blue** and text deletions are in **red**.

### Specific Comments

Section	Line No.	Comment and Rationale	Proposed rewording (if applicable)
2.1.1	63-64	Requiring instrument calibration and system suitability measurements to follow the regional requirements would undermine the ability to use and reference the methods interchangeably. The elimination of this section does not adversely affect the methods' capabilities to demonstrate that a test article does/does not comply with the acceptance criteria for any region.	<del>2.1.1 Instrument calibration and system suitability measurements should follow regional GMP requirements.</del>
4.1	79-82	The regulatory mechanisms for notifying regional authorities when sponsors or manufacturers change their existing methods to the implemented Q4B-evaluated pharmacopoeial texts in accord with Section 2. of the annex should be harmonized. As this annex confirms, at Step 5 of the evaluation process, regional regulatory acceptance of the interchangeability of the analytical procedures and/or acceptance criteria (APAC) in all regions, such a harmonized notification mechanism should require neither a review period nor approval.	General consideration: When sponsors or manufacturers change their existing methods to the implemented Q4B-evaluated pharmacopoeial texts that are referenced in Section 2.1 of this annex, any change notification, <del>variation, and/or prior approval procedures should be handled in accordance with established regional regulatory mechanisms pertaining to compendial changes</del> made to the appropriate regional authorities shall not require either a review period or approval by the regional authorities.
4.4	98-101	Same comment as for Section 4, line numbers 79-82	4.4 MHLW consideration: The pharmacopoeial texts referenced in Section 2.1 of this annex can be used as interchangeable in accordance with the conditions set out in this annex. <del>Details of implementation requirements will be provided in the notification by MHLW when this annex is implemented.</del>

