

Samata Veluvolu
Manager, Regulatory Affairs

January 15, 2009

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

Re: Docket No. FDA-2008-D-0559; Draft Guidance for Industry on Process Validation: General Principles and Practices; Availability

The ANIMAL HEALTH INSTITUTE ("AHI") submits these comments to FDA-2008-D-0559; Draft Guidance for Industry on Process Validation: General Principles and Practices; Availability. AHI is the national trade association representing manufacturers of animal health products -- the pharmaceuticals, biological products and feed additives used in modern food production, and the medicines that keep livestock and pets healthy. AHI member companies represent the majority of animal pharmaceuticals and animal insecticides, as well as serving a significant segment of the world market. As such, we have a tremendous interest in the principles used in validating a manufacturing process for animal drugs.

AHI members are concerned that the thoughts presented in the guidance do not take into consideration veterinary process validation. Since this is a joint guideline issued by CDER, CBER and CVM, we need some clarification as to what will actually be required versus "nice to have" for animal health companies. There are typically more stringent requirements for CDER and CBER that may not apply to CVM. Many comments in the guidance refer to the concept of "Quality by Design", and some specifically to the use of process analytical technologies. While FDA has been trying to move industry for some time now to create more process knowledge during the development phase, it is somewhat unclear how far these requirements go. The use of PAT, for instance, is at this time strictly voluntary. AHI members would like to know what CVM's expectations are for animal health companies fulfilling these requirements and request clarification on the extent to which manufacturers of animal health products should follow the guidance.

Contrary to human pharmaceutical development, the veterinary industry does not go through development phases 1 - 3, and as a consequence, fewer process development batches are manufactured. This is also in line with the need to keep development costs much lower compared to human Pharma because of the much smaller veterinary market size. However, the pressure to move quickly through the development is the same.

AHI has several general and specific suggestions to include in the guidance which would bring more clarity to the animal health industry:

General Suggestions:

- Process Validation Decision Tree
- Definitions Section

- Schematic showing the relationship between IQ/OQ/PQ to Process Design/Process Qualification/Process Verification/Process Validation
- Specific (veterinary) examples of processes that do/do not require process validation

Specific Suggestions / Clarification:

- Include more specific (veterinary) examples throughout the document
- Requirements of a veterinary Process Validation submission data package
- Examples of when concurrent validation is acceptable, as the manufacturing of validation lots may be spread over by as much as 5 years if the veterinary product is low demand and/or seasonal
- Examples of situations where concurrent release is appropriate for veterinary drugs (as we do not have orphan drugs)

Additional, specific comments and questions on the draft GFI are provided in the attached table.

Thank you in advance for your consideration of these comments. Should you have any questions, please do not hesitate to contact AHI at (202) 637-2440.

Sincerely,



Samata Veluvolu
Manager, Regulatory Affairs

Date:	Document:
January 15, 2009	GFI: Process Validation: General Principles and Practices

Commenter	Page No. and/or Section	Line No.	Text	Comments/Questions
AHI	General			We request clarification on the extent that the veterinary industry should follow this guidance document.
AHI	General			How do you differentiate between new drug development and old drug development? Would we apply the same principles for the transfer of an old product to a new site as we would for a new product? The concept of process design is fine if we are developing a product for the first time, but if we have an old product and historical data that supports the processes and controls, will that be sufficient, or do we have to show the requirements for a new drug?
AHI	General			Please provide examples where validation is necessary when changes in non-critical parameters are implemented.
AHI	General			How should validation information created during the design phase be submitted? As part of the development report and separately from the validation (referred here as "stage 2" or "performance qualification") after approval and before product launch?
AHI	Page 2	Subscript 3	Process validation for APIs is discussed in the FDA/ICH guidance for industry, <i>Q7A Good Manufacturing Practice Guidance for Active Pharmaceutical Ingredients</i> (ICH Q7A)...	It is stated that API or drug substances are within the scope of this guidance. However, the text indicates that process validation for APIs is discussed in Q7A. Q7A does not go into the detail regarding process validation that this guidance (196) goes into. Q7A has a general chapter (XII) entitled "Validation" which discusses validation policy, documentation, qualification, approaches, validation of analytical methods, periodic review of validated systems, process validation and cleaning validation. Did FDA cite Q7A for completeness?
AHI	Page 7 Section IV	Lines 255-256	...as well as the contributions of variability by different component lots...	Is the use of different batches of API and excipients required or nice to have? The wording of the text increases the scope of what is normally done in the veterinary industry. Since validation shows understanding of the process, it should not matter how many batches we use as long as we can justify using more or less. Pharma drugs usually have more development-type batches.

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January 15, 2009	GFI: Process Validation: General Principles and Practices

Commenter	Page No. and/or Section	Line No.	Text	Comments/Questions
AHI	Page 9 Section IV	Lines 333-334	It is essential that activities performed to assure proper facility design and commissioning precede PQ.	Does this mean that if a facility's design is established for a specific product, it does not need to be established again for another product manufactured at the same facility?
AHI	Page 10 Section IV	Lines 389-390	Previously credible experience with sufficiently similar products and processes can also be considered.	If a process was validated and just the organism and the media changed, would CVM accept data from the previous validation? For example, if a fermentation manufacturing process is validated to produce a particular product, can this validation data be used to support the manufacture of another fermentation product using exactly the same equipment? The only difference being the fermentation medium and microorganism?
AHI	Page 14 Section IV	Lines 533-535	We recommend continued monitoring and/or sampling at the level established during the process qualification stage until sufficient data is available to generate significant variability estimates.	This could have exceptions if the PQ is designed appropriately.
AHI	Page 15 Section V	Lines 584-586	We recommend each batch in a concurrent release program also undergo stability testing and that this test data be promptly evaluated to ensure rapid detection and correction of any problems.	AHI members believe if, for some reason, there were multiple lots in the PQ stage being concurrently released, it could be justified to exclude some lots from stability. It would pose a hardship to animal health companies for each batch to have to undergo stability testing.
AHI	Page 16 Section VII	Lines 620 – 623	While validated analytical methods are not required during product- and process-development activities, methods should be scientifically sound (e.g., specific, sensitive, and accurate), suitable and reliable for the specified purpose.	API process development activities and analytical methods development are typically done at the same time, each function supporting the other. Therefore, analytical methods cannot be specific and accurate prior to completing development. Therefore, it is suggested to revise this text to remove “specific” and “accurate” words.
AHI	Page 16 Section VII	Lines 626-627	Analytical methods supporting clinical supply production, particularly stage 2 and 3 studies, must follow appropriate CGMPs in parts 210 and 211.	As indicated previously, the veterinary industry does not go through development phases 1 – 3. Therefore, clarification is sought. It is suggested to add “analytical methods supporting release of veterinary products and APIs that will be used in the clinical studies must follow appropriate CGMPs in parts 210 and 211”.