29 March 2019

Health Product Inspection and Licensing Division
Health Canada
13th Floor, Jeanne Mance Building
200 Eglantine Driveway, Tunney's Pasture
Ottawa Ontario K1A 0K9
Canada

Reference: Good manufacturing practices for active pharmaceutical ingredients (GUI-0104)

Dear Madam or Sir:

PDA appreciates the opportunity to comment on the revised draft guidance on good manufacturing practices for active pharmaceutical ingredients (GUI-0104). We present our comments in Table 1, attached.

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 have been prepared by a committee of PDA members with expertise in pharmaceutical and biopharmaceutical manufacturing on behalf of PDA’s Regulatory Affairs and Quality Advisory Board and Board of Directors.

If you have any questions, please do not hesitate to contact me via email at johnson@pda.org.

Sincerely,

Richard Johnson
President and CEO

cc: Tina Morris, PDA; Ruth Miller, PDA
December 31, 2018

SUBJECT: Consultation Comment Form

Dear Stakeholder,

Health Canada is conducting a consultation on the following draft guidance document. The consultation will be open for 90 days from December 31, 2018 to March 31, 2019.

- GUI-0104: Good manufacturing practices for active pharmaceutical ingredients

Please email your comments to hc.api.questions-ipa.sc@canada.ca, using this form. All comments will be considered in the finalization of the document. The 90-day consultation period is from December 31, 2018 to March 31, 2019, inclusive.

Comments can also be mailed to:

Health Product Inspection and Licensing Division
Health Product Compliance Directorate
13th Floor, Jeanne Mance Building
200 Eglantine Driveway, Tunney's Pasture
Address Locator # 1913D
Ottawa Ontario K1A 0K9

Sincerely,

Health Product Inspection and Licensing Division
Comment Form

Optional Contact Information:

Name: Richard Johnson
Title: President and CEO
Organization/Company: Parenteral Drug Association
Address: 4350 East West Highway, Suite 600
City: Bethesda
Province: MD, USA
Postal Code: 20814
Email Address: johnson@pda.org

Step 1: Enter the title and number of the guidance document for which you are providing comments.
  Good manufacturing practices for active pharmaceutical ingredients [GUI-0104]

Step 2: Complete Table 1 which can be found on the next page by indicating the line number, page number, current text, proposed revision or comments, and a rationale. You may add additional lines as required.
<table>
<thead>
<tr>
<th>Line Number</th>
<th>Page Number</th>
<th>Current Text</th>
<th>Proposed Revision or Comments</th>
<th>Rationale</th>
</tr>
</thead>
</table>
| 126         | 8           | The guidance in this document has been written with a view to harmonize with GMP standards from:  
  - the International Conference on Harmonisation (ICH)  
  - the Veterinary International Conference on Harmonisation (VICH)  
  - the Pharmaceutical Inspection Cooperation/Scheme (PIC/S)  
  - other international regulatory agencies                                                                 | PDA agrees with this objective, but suggests that Health Canada’s efforts at harmonization with ICH and PIC/S would be clearer if the agency were to update the prior version of GU-0104 without completely rewriting it as proposed. While in many cases PDA supports the use of plain language in regulatory documents, such language should be adopted carefully and discretely when referencing globally harmonized language. We highlight below some specific and meaningful differences in wording between this revision and ICH Q7, but have not attempted to comprehensively identify all potential issues that may arise as regulated entities work through this document.  
As an alternative, Health Canada might consider adopting ICH Q7 verbatim, then editing GU-0104 to describe only Canada-specific topics such as site licensing for biologics and narcotics.                                                                 | ICH Q7 and the PIC/S Guide to Good Manufacturing Practices for Medicinal Products Part II are harmonized. This draft guidance's departure from the language of those harmonized documents presents challenges for companies that operate globally, which is particularly significant in the area of API. This revision could inadvertently bring about disharmonization due to the differences in the language used in this revised document. |
<p>| 126         | 9           | This version reflects recent regulatory amendments, clarifies existing requirements...                                                                                                                                 | PDA suggests that Health Canada’s intentions would be clearer if the agency were to update the prior version of GU-0104 but not completely rewrite it as Health Canada has proposed.                                                                                                                                                                                                                                  | By attempting to provide clarity through the use of plain language, Health Canada may instead raise confusion about the GMP requirements for APIs under Canadian law vs. the requirements of other... |</p>
<table>
<thead>
<tr>
<th>Page</th>
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<tbody>
<tr>
<td>261</td>
<td>Regular quality reviews of APIs should be conducted with the objective of verifying the consistency of the process and should be documented.</td>
</tr>
<tr>
<td>319</td>
<td>Provide good ventilation, air filtration and exhaust systems.</td>
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<td>120</td>
<td>21</td>
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<td>105</td>
<td>7</td>
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