

## Amgen, Inc Comments on ICH Topic Q8, Step 2 Note for Guidance on Pharmaceutical Development US FDA Docket 2005D-0021

General Comments
<p>It is not entirely clear whether the guideline is intended to apply biotech products as well as New Chemical Entities (NCEs). All of the specific guidance provided is aimed at NCE products yet it is stated in Section 1.3. that it is intended to apply to all products within the scope of Module 3 of ICH M4. Module 3 of ICH M4 applies to both biotech and NCE products and if this is also intended to be the scope of ICH Q8, there needs to be much more effort put into providing appropriate guidance for biotech products.</p>
<p>In various sections, references are made to 'flexible regulatory approaches' ie, reducing the need for submission of variations/supplements following some product and process changes on the basis of information gathered during development (or subsequently) and provided in the application. However, it is unclear how this would work in practice.</p>
<p>Overall, the guidance was written in a general way and left much open for interpretation. Text should be more specific when possible.</p>

Specific Comments			
Item with Reference Line #	Relative Importance	Key Concerns with Explanation of Position	Proposed change
<p>Section 2, 6th Paragraph Lines 68-79</p>	<p>Minor</p>	<p>It is stated that the applicant may choose to conduct additional pharmaceutical development studies that allow the establishment of a 'design space' within which the process may be changed, without necessarily triggering variations. Formal experimental designs or data gathered through Process Analytical Technologies (PAT) approaches are mentioned as the means of establishing the design space. It would be unrealistic to expect that a sufficiently large body of data would be available at time of filing to support the definition of a design space.</p>	<p>It may be appropriate in this section (and throughout) to give some indication as to what data is expected at initial filing and what would more likely be gathered and presented post-authorization.</p>
<p>Section 2.3. 5th Paragraph Lines 258-260</p>	<p>Minor</p>	<p>It is unclear what is meant by 'structured risk management tools'. This term is not defined in the glossary.</p>	<p>Define term "structured risk management tools"</p>
<p>2.0 Pharmaceutical Development I Lines 61-63</p>	<p>Minor</p>	<p>Appear to allow control <u>OR</u> monitoring of critical parameters.</p>	<p>Need to clarify. Critical parameters are In Process Controls (IPCs), which require rejection limits. Monitoring of these parameters alone is insufficient.</p>