Final, 28th July 2014

Submission of comments on the EMA/CHMP/CVMP/QWP [Concept paper on the need for a single note for guidance on the chemistry of active substances](http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2014/02/WC500161109.pdf" \t "_blank) (EMA/CHMP/QWP/752676/2013)

Comments from:

| Name of organisation or individual |
| --- |
| EFPIA |

*Please note that these comments and the identity of the sender will be published unless a specific justified objection is received.*

*When completed, this form should be sent to the European Medicines Agency electronically, in Word format (not PDF).*

1. General comments

| Stakeholder number  *(To be completed by the Agency)* | General comment (if any) | Outcome (if applicable)  *(To be completed by the Agency)* |
| --- | --- | --- |
|  | EFPIA welcomes this Concept Paper for the development of a new Guideline that will combine and replace the following two documents: CPMP/QWP/130/96-Rev1 and 3AQ5a. |  |
|  | **Scope of the new GL**: the Concept Paper lacks specifications that the new guideline will continue to apply to new active substances only, as is the case for the two existing ones. This should be clearly reflected in the title of the new guideline.  The new GL should also address the different types of active substances manufacturing methods, i.e. synthesis, semi-synthesis, fermentation, extraction, and/or the types of molecules, e.g. antibiotics, fermentation products, herbal drugs, oligopeptides, oligonucleotides and oligosaccharides. For instance with regard to oligopeptides, the Ph. Eur. general monograph “substances for pharmaceutical use” that is used to establish such active substance specification could be referred to. |  |
|  | **ICH Q11**: the “enhanced approach” described in ICH Q11 guideline is supported by both industry and regulatory authorities and should be promoted further in the revised GL, especially on how it translates into the entire CMC dossier structure, taking into account that ICH Q11 guideline is mainly focused on 3.2.S.2.2 to 3.2.S.2.6 sections of the CMC dossier. Besides, it would be useful if the same kind of guidance as the one proposed in the current concept paper for chemistry be envisaged for the biotechnological / biological entities, equally reflecting ICH Q11 guideline. |  |
|  | **Subsequent NTA update**: the NTA 2B, CTD-Module 3, edition July 2004, refers to both current GLs, while still containing some (duplicate) information related to NCEs. Thus, it would make sense to update the NTA also, by only providing a reference to the revised GL. |  |

1. Specific comments on text

| Line number(s) of the relevant text  *(e.g. Lines 20-23)* | Stakeholder number  *(To be completed by the Agency)* | Comment and rationale; proposed changes  *(If changes to the wording are suggested, they should be highlighted using 'track changes')* | Outcome  *(To be completed by the Agency)* |
| --- | --- | --- | --- |
| 3. Discussion (on the problem statement) |  | **Comment**: lines 6 & 7 should further clarify that the guideline will apply to both ‘traditional’ and ‘enhanced’ approaches.  **Proposed change**: ”It will be clarified that this guideline is applicable to applications which follow the “traditional” approach and not the “enhanced” approach**es.** which is also included***The enhanced approach is further discussed*** in ICH guideline Q11 on development and manufacture of drug substances.” |  |
|  |  | **Comment**: it is not clear whether specifications for Genotoxic Impurities will be fully captured in the revised guideline, or whether the existing EU guidance and respective Q&A will be updated accordingly. |  |
|  |  | **Comment**: since not addressed in the existing guidelines (CPMP/QWP/130/96-Rev1 and 3AQ5), the new GL should probably address the reworking and recovery of materials and solvents (in addition to the reprocessing), and based on ICH Q7 definitions. |  |
| 9. References |  | CTD:regarding the CTD format, a reference to ICH M4 may be appropriate. |  |
|  |  | Genotoxic impurities:  For chemically synthesised peptides and oligonucleotides, ICH S6 on ’Pre-clinical safety testing requirements for biotech products’ could be referred to.  Also a reference to the CHMP SWP Reflection Paper on the Assessment of Genotoxic potential of antisense oligodeoxynucleotides (EMEA/CHMP/SWP/199726/2004) may also be useful. |  |
|  |  | Considerations for ICH references, pending status/public release:  - M7 on ‘Genotoxic impurities’ and  - Q3D on ‘Elemental impurities’ |  |