IPEC Europe notes the AESGP position paper drafted in August 2009. On the whole the presentation is logical and in accordance with the EMEA Q&A on atypical actives. There are some aspects that we feel could be better elaborated.

We feel that a strong definition of an Atypical Active is required at the start of the document. We offer one in out appended Q&A paper on this topic. We also emphasise in our definition that a Marketing Authorisation has already been granted in order for the API to be qualified as “Atypical”. Thus we feel it should be emphasised that a new marketing authorisation would only utilise an “Atypical Active” under the most extreme of circumstances.

In relation to the AESGP position paper drafted in August 2009, the arguments in the following paragraph on page 1 could be better presented:

“As a result, choices are limited to either find a GMP compliant supplier - provided that one exists - with all the re-validation work and cost entailed, or to withdraw the product containing the substance. Either option are far from being workable for the self-care sector as non-prescription medicines are usually cheap and in most part produced by small and medium sized enterprises. Thus, an increase in the production cost or a loss of product in their portfolio may not be bearable.”

It is difficult for IPEC Europe to suggest alternative wording to this paragraph. However, to limit the argument to one of simple business costs is inappropriate when the intent of the regulations is to assure patient safety, firstly from the medicines themselves and secondly by making those medicines available. If this factor really is that critical then an argument along the lines of the one developed in the Europe Economics Report on the Certain Excipients issue would be more balanced.¹

We feel that the AESGP list of Atypical Actives should be updated (perhaps in the latest document) to indicate that some substances are now available from suppliers in compliance with Part II GMP.

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In the recommendations for medium term action by the authorities we suggest bullet 5 be reworded, from:

“5. The dosage form manufacturer or MAH should perform audits of the starting material manufacturer (these should preferably be on site, but if access is not allowed then a paper audit will need to be performed). The audits should be against the requirements of Part II of the GMP Guide with the main focus upon control of the key parameters and conformance to specification.”

IPEC Europe suggests this paragraph be developed from the viewpoint of the regulatory authorities. In this the Atypical Active Manufacturer should agree to implement a defined standard of GMP. IPEC Europe suggests that in many cases the IPEC-PQG GMP Guide would be a credible minimum definition of that GMP, especially where the Atypical Active is already made as an Excipient.

This would indicate other options than a physical or paper audit are open.

In this respect the risk assessment indicated in Bullet 6 would be simpler to complete as the differences between PART II and the IPEC-PQG GMP Guide are already defined.

We recognise that several IPEC Europe members who manufacture excipients have now discovered that these are Atypical Actives. In such cases where the starting material manufacturer agrees to continue supply for this purpose IPEC Europe agrees with bullet 4, which recommends that the supplier and user confirm this in an agreement. The agreement should acknowledge that the current GMP being implemented by the starting material manufacturer is acceptable to the user.

In the medium term it would be preferable to allow Atypical Actives to be acceptable in law. As this would require a major change in legislation, it may be better to allow the status quo to continue. However we feel that use of an Atypical Active in a new marketing authorisation should only be allowed in very exceptional circumstances.

Where these comments can be accommodated, IPEC Europe finds the document reflects a suitable approach that is in line with the EMEA Q&A paper and current regulatory expectations.