Dear Sirs

Below please find some remarks to point 3.6 (chapter 3 GMP guideline revision proposal):

In this point you can find the statement:

Dedicated facilities are required for manufacturing when a medicinal product presents a risk:

a) Which cannot be adequately controlled by operational and/ or technical measures or
b) **Scientific data does not support threshold values (e.g. allergenic potential from highly sensitizing materials such as beta lactams) or**
c) Threshold values derived from the toxicological evaluation are below the levels of detection

It **must be pointed out** that data for beta-lactams anafilitic reaction threshold exist. **Moreover** this threshold is presented in **EMEA** document:

http://www.ema.europa.eu/docs/en_GB/document_library/Maximum_Residue_Limits_-_Report/2009/11/WC500015568.pdf
Committee for Veterinary Medicinal Product: Penicillins Summary Report Revision 1 (2008)

The threshold value for penicillin indicated there is 6 mcg (10 UI of penicillin). Although it concerns residuals in meat and milk it is valuable to use it in risk evaluation of beta-lactams medicinal products with **oral administration route**. Normally medicinal products are not taken on pernament matter so the danger from beta-lactams residuals in food in certain cases seems to be even more significant.

As the cephalosporins has a similar mechanism of anaphylactic reaction it can be also useful to evaluate risk here.

There is no doubt that critical manufacturing steps like mixing, granulating, tabletting and coating should be done id dedicated area. But final manufacturing steps where no beta-lactams dust is produced (e.g. packaging of coated tablets) could be possible in not dedicated manufacturing area after appropriate risk management, operational and technical measures.

Best regards

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