

Divergent position on a final CVMP opinion on an Article 13 referral of Commission Regulation (EC) No 1234/2008 for

Soludox 500 mg/g powder for use in drinking water for pigs and chickens (EMA/V/A/090)

The marketing authorisation holder has applied for a shorter withdrawal period for chicken meat and offal for Soludox 500 mg/g powder for use in drinking water for pigs and chickens, when the product is administered at the dose of 20 mg/kg bw for 4 consecutive days. Currently the withdrawal period is 12 days, the marketing authorisation holder is applying for 6 days. The marketing authorisation holder has delivered two residue depletion studies, one from 1999 and another from 2011. The study from 1999 is leading to a withdrawal period of 12 days, whereas the 2011 study leads to a withdrawal period of 6 days using the statistical approach. The CVMP has combined the 2 studies and recommended a withdrawal period of 9 days.

The undersigned cannot support this conclusion due to the following facts:

- It is not appropriate to combine the two studies as they may have been conducted under different conditions. It is well documented that the bioavailability of doxycycline can vary from study to study because of variation in feed composition. The two studies present difference in water consumption and feed intake and feed composition.
- Different analytical methods have been used. In 1999 analyses have been based on water standards corrected for matrix effect. In 2011 analyses have been based on tissue matrix and by use of an internal standard. The limits of quantification and limits of detection are different in the two studies with the lower ones in the 2011 study. The limit of quantification is half the MRL in the 1999 study and a quarter of the MRL in 2011.
- All tissue samples could be measured in the 2011 study but not in the 1999 study which is related to the difference in limit of quantification. For example in muscle 3 samples out of 6 could not be quantitated at Day 5 and 2 out of 6 at Day 8. This leads to conversion of these samples to values equivalent to half the MRL affecting the outcome of the calculation of the withdrawal period.
- Since doxycycline is soluble to the same extent in all doxycycline salts, it does not make sense to have different withdrawal periods for different products. The majority of products have a withdrawal period of 5 days.
- Since the study from 2011 could determine all tissues and therefore gives a more realistic picture of doxycycline tissue depletion the undersigned concludes that this study gives more reliable measure than the study from 1999. Consequently I consider that the withdrawal period of 6 days would be appropriate.

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