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International Cooperation on Harmonisation of Technical Requirements for Registration of Veterinary Medicinal Products

VICH GL21 (ANTHELMINTICS CHICKENS – *Gallus gallus*)
October 2024
Revision 1 at Step 9
For Implementation at Step 7

EFFICACY OF ANTHELMINTICS: SPECIFIC RECOMMENDATIONS FOR CHICKENS – *Gallus gallus* (REVISION 1)

Revision at Step 9

Adopted at Step 7 of the VICH Process by the VICH Steering Committee
in October 2024
for implementation by October 2025

This Guideline has been developed and revised by the appropriate VICH Expert Working Group in accordance with the VICH Process. At Step 7 of the Process the final draft is recommended for adoption to the regulatory bodies of the European Union, Japan and the USA.

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EFFICACY OF ANTHELMINTICS: SPECIFIC RECOMMENDATIONS FOR CHICKENS - *Gallus gallus*

INTRODUCTION

The present guideline for chickens (*Gallus gallus*) was developed by the Working Group established by the Veterinary International Cooperation on Harmonization (VICH), Anthelmintic Guidelines. It should be read in conjunction with the VICH Efficacy of Anthelmintic: General Requirements Guidelines (VICH GL7) which should be referred to for discussion of broad aspects for providing pivotal data to demonstrate product anthelmintic effectiveness. The present document is structured similarly to VICH GL7 with the aim of simplicity for readers comparing both documents.

The aim of this guideline for chickens is (1) to be more specific for certain specific issues for chickens not discussed in VICH GL7; (2) to highlight differences with VICH GL7 on efficacy data requirements and (3) to give explanations for disparities with VICH GL7. We recommend to the sponsors to refer to the pertinent procedures described in detail in other published documents e.g., World association for the advancement of veterinary parasitology (WAAVP): Second edition of guidelines for evaluating the efficacy of anthelmintics in poultry. *Veterinary Parasitology* 305: 109711, 2022, and updated versions as they are published.

For other poultry, the principles outlined in this guideline should be used where applicable.

A. General Elements

1. The Evaluation of Effectiveness Data

Only controlled tests based on parasite counts of adults/larvae are acceptable both for the dose determination and dose confirmation studies, since critical tests generally are not considered to be reliable for chickens. Egg counts with identification of the genus is the preferred method to evaluate the effectiveness in field studies. Adequate parasite infection should be defined in the protocol according to regional prevalence or historic data and/or statistical analysis.

2. Use of Natural or Induced Infections

Dose determination studies generally should be conducted using induced infections with either laboratory strains or recent field isolates.

Dose confirmation studies could be conducted using naturally infected birds which can have superimposed induced infections. This procedure will allow a wide range of parasites to be present in the experimental birds. Also induced infections in one of the studies is acceptable. Studies for larval stages should be conducted with induced infections only.

The history of the parasites used in the induced infection studies should be included in the final report.

3. Number of Infective Forms Recommended for Induced Infections

Table 1 indicates the number of eggs/cysticercoids recommended to be used and will depend on the isolate that is used. The final number of eggs/cysticercoids used in the infection should be included in the final report.

Table 1. Range of Infective Stages Used to Produce Adequate Infections in Chickens for Anthelmintic Evaluation.

Parasites	Range
Ascaridia galli	200 - 500
Capillaria obsignata	100 - 300
Heterakis gallinarum	200 - 300
Raillietina cesticillus	50 - 100
Syngamus trachea	200 - 600

Some factors to consider for induced infections in chickens are:

a) Young birds should be used in the studies;

b) To maximize the establishment of adequate infections it is recommended to use low numbers of infective stages;

c) Stress (e.g., poor diets) is not required to generate helminth infections;

d) Housing conditions should not allow accidental infections.

4. Recommendations for the Calculation of Effectiveness

4.1 Criteria to Grant a Claim

To be granted a claim, the following pivotal data should be included:

a) Two dose confirmation studies conducted with a minimum of 6 adequately infected experimental units (individual birds or pens, see Glossary) in the non-medicated control group in each study. The infection of the experimental units in the study will be deemed adequate based on historical, parasitological and/or statistical criteria.

b) The differences in parasite counts between treated and control experimental units should be statistically significant ($p \leq 0.05$).

c) Percent efficacy should be 90% or higher and calculated and interpreted as described in Section 4.5 of VICH GL7.

4.2 Number of Experimental Units in Dose Determination and Dose Confirmation Studies

The minimum number of experimental units required per experimental group is a crucial point. Although the number of experimental units will depend on the possibility to process the data according to an adequate statistical analysis, it has been recommended, to achieve harmonization, that the inclusion of at least 6 experimental units in each experimental group is a minimum.

4.3 Adequacy of Infection

The minimum adequate number of helminths in individual control birds should be defined in the protocol. However, final conclusions regarding adequacy of infection will be made as part of the final report based on statistical analysis, historical data, literature review, or expert testimony. If the experimental unit is a pen, an adequately infected pen should be defined by a minimum number of adequately infected birds out of the total number of birds in the pen (i.e.,

percentage of adequately infected birds in the pen).

The range of chicken helminths (adults) considered adequate to grant a claim will vary according to the species[1]. Generally, a minimum of 20 *A. galli* in individual control birds is considered an adequate infection. Lower counts may be expected with *H. gallinarum*, *C. obsignata* and *R. cesticellus.* Necropsies should be conducted within 10 days after treatment.

4.4 Label Claims

For adult claims, as a general rule, the treatment should not be administered earlier than 28 days after infection. It is recommended to include at least 6 sentinel birds for helminth characterization and quantification before treatment is initiated. For L4 claims, treatments should be given, as a general rule, 7 days after infection, except for *A. galli* and *H. gallinarum* which should be 16 days after infection.

5. Treatment Procedures

The method of administration (oral, parenteral, topical, slow release etc.), formulation and extent of activity of a product will influence the protocol design.

When the drug is to be administered in the water or in a feed, it should be done as much as possible following the labelling recommendations. Palatability/consumption studies may be required for medicated feeds. Samples of medicated water or medicated feed should be collected to confirm drug concentration. The amount of medicated product provided to each animal should be recorded to ensure that the treatment satisfies the label recommendations.

6. Bird Selection, Allocation and Handling

Test birds should be clinically healthy and representative of the age, sex, and class for which the claim of the test anthelmintic is to be made. In general, birds should be young and from a breed that is susceptible to helminth infections. If birds are housed in pens (e.g., cages or floor pens), the birds should be randomly assigned to each pen. The experimental units should also be randomly assigned to each treatment group. Randomization to treatment group should be performed using an adequate method that should be described in the protocol and final report. Blocking should only be employed if it is expected to reduce residual error in the study. If blocking is used, blocks should be included as a random effect in the statistical model. Nevertheless, blocking is not always the most appropriate method for reducing residual error. Alternative methods may therefore be considered e.g., a suitably selected covariate.

Animal housing, feeding and care should follow strict requirements of welfare, including vaccination according to local practices. This information should be provided in the final report. A minimum acclimatisation period of 10 days is recommended. Housing and feed/water should be adequate according to the geographical location. Birds should be monitored daily for adverse reactions.

B. Specific Evaluation Studies

1. Dose Determination Studies

If the treatment requires extended administration, one or more studies are required to determine the minimum treatment period for efficacy.

[1] The recommended minimum numbers are based on a review of published literature and data from studies submitted for regulatory review.

2. Dose Confirmation

No species-specific recommendations.

3. Field Efficacy Studies

Depending on the facilities available, the experimental unit may be the animal, pen, or the shed/house (see glossary). The design of the field studies should represent current commercial conditions and should be replicated in different geographic locations and in different production class(es), depending on the indication being pursued. Housing will differ based on the production class under investigation (e.g., layers vs. broilers). The protocol should state the number of experimental units per treatment group (sample size), describe allocation (proportion) to treatment groups, and include a brief description of how the sample size was determined. Regardless of whether one or multiple parasites are being evaluated within a study, an appropriate sample size calculation or justification is necessary prior to study conduct.

When commercial facilities (or similar) are used, the shed/house should be subdivided, when possible, to allow for sufficient replication to enable a statistical analysis. If the shed/house is the experimental unit and there is only one replicate per treatment group at a study site, the study may need to utilize additional sites with the same housing conditions to achieve sufficient replication and enable a statistical analysis. Otherwise, a study with one replicate can only be summarized using descriptive statistics and may not provide sufficient inferential value.

Effectiveness should be assessed by the reduction of worm counts in all birds or in representative birds as determined by comparing the treated and control groups. If representative birds are used for worm counts the protocol should describe procedures for random selection of animals (number and percentage) to be necropsied. Faecal egg counts may be used to establish pre-treatment infection levels and parasite species present. A comparison of pre- and post-treatment faecal egg counts may be included but is not required. If faecal egg counts are evaluated, fresh, clean droppings should be collected immediately before treatment, and at 7 to 14 days after treatment. The faecal sampling method, number of pens/animals sampled, and egg counting technique should be defined in the protocol. Standard, well accepted techniques should be used and fully described in the protocol and final report.

Clinical observations, production variables, and records of culls and mortality should be maintained and compared to control birds and historical data of the commercial establishment. If birds are processed at the end of the study, slaughterhouse inspection reports with final observations regarding possible abnormalities which are collected per the standard practices of the slaughterhouse should be included in the final report. However, if the study duration does not coincide with or include slaughterhouse processing, these data are not required.

GLOSSARY

EXPERIMENTAL UNIT: The entity (e.g., individual animal, cage, pen, or shed/house) which can be independently and randomly assigned to a treatment, and whose response to the assigned treatment can be independently evaluated. The experimental unit is the basic unit for the statistical analysis. The experimental unit may be the individual bird or the pen/shed/house depending on the circumstances of the study:

1) The pen/shed/house is the experimental unit in the analysis if all birds in a pen/shed/house are provided the same treatment through medicated feed or water; or

2) The individual bird is the experimental unit in the analysis if the treatment can be individually administered, the treatments are randomly assigned to birds within a pen/shed/house, and the endpoint can be evaluated independently for each bird in a pen/shed/house.