US Environmental Protection Agency
Office of Pesticide Programs

Lower Certified Limit Testing Guidance

December 6, 2013

Guidance For Efficacy Testing at the Lower Certified Limits

Notice to: Manufacturers, Producers, Formulators and Registrants of Pesticides

Attention: Persons Responsible for Federal Registration and Registration of Pesticide Products

Subject: Active Ingredient Concentration Standards for Efficacy Testing

Purpose: The purpose of this notice is to define the Agency's criteria for efficacy testing at the active ingredient lower certified limit(s) for antimicrobial products.

I. BACKGROUND

One of the Agency's goals is to ensure that all antimicrobial products are efficacious at any active ingredient concentration within the approved certified limits. In order to meet this objective, a comprehensive testing strategy that evaluates product efficacy at the lower certified limit(s) is deemed necessary by the Agency. In accordance with this assessment approach, the recently revised 810 series guidelines indicate the need for efficacy testing to be performed with the active ingredient concentration(s) at the lower certified limit(s) for each active ingredient in the tested product [810.2000 (e)(1)(i)]. The purpose of this notice is to define the scenarios under which efficacy testing at the lower certified limit (LCL) is needed. This document also defines the allowable range above the LCL that may be used for testing in situations where product sample at the exact lower certified limit cannot be obtained.

II. LCL TESTING REQUIREMENTS

As indicated, efficacy testing at the LCL is necessary to demonstrate an antimicrobial product's ability to consistently perform as labeled. It is the Agency's view, however that not all efficacy data submissions necessitate testing at this concentration. Table 1 identifies the types or classes of efficacy data which should include testing at the LCL, as well as circumstances where testing at or below the nominal concentration is considered appropriate. As described below, testing at the lower certified limit(s) should be performed for all of the required microbial organisms supporting a specific efficacy class. Lower certified limit testing of additional organisms should also be included for the tuberculocidal, sterilant/sporicidal, and food-contact sanitizer efficacy classes. The LCL testing standards for fungicidal disinfection will be addressed under a separate notice.

Table 1. Lower Certified Limit (LCL) Efficacy Testing Criteria

Efficacy Class (see appropriate 810 guideline for required microbe)	LCL Testing	
	New Registration Submission	Amendments to Registered Product
Disinfection (Hospital, Broad or Limited-Spectrum):		
Required Microbes	Test at LCL	Test at LCL
Additional Microbes (except CRE)	Not needed	Not needed
Carbapenem-resistant *Enterobacteriaceae* (CRE)	Test at LCL	Test at LCL
Tuberculocidal Disinfection:		
Required Microbe and Additional Microbes	Test at LCL	Test at LCL
Fungicidal Disinfection:		
Required Microbe	Reserved	Reserved
Virucidal Disinfection:		
Required Virus: Hardest to Kill strain [See 810.2200(f)]	Test at LCL	Test at LCL
Additional Viruses: Easier to Kill strains [See 810.2200(f)]	Not needed	Not needed
Non-Food Contact Sanitizer:		
Required Microbes	Test at LCL	Test at LCL
Additional Microbes (except CRE, e.g. MRSA, *E. coli*)	Not needed	Not needed
Carbapenem-resistant *Enterobacteriaceae* (CRE)	Test at LCL	Test at LCL
Food Contact Sanitizer:		
Required Microbes and Additional Microbes	Test at LCL	Test at LCL
Sterilant/General Sporicidal:		
Required Microbes and Additional Microbes	Test at LCL	Test at LCL
***Clostridium Difficile* -Sporicidal:**		
Required Microbe	Test at LCL	Test at LCL

Note that this guidance for LCL testing applies to all three batches tested in the subject study. Consultation with the Agency prior to the initiation of testing is recommended for types of efficacy data that do not fall into the classes identified in Table 1. Furthermore, this listing may be revised to address LCL testing for other microbial organisms as the Agency's concerns change regarding emerging pathogens.

III. ACTIVE INGREDIENT CONCENTRATION STANDARDS

The Agency is aware of the potential difficulties associated with generating test samples exactly at the lower certified limit. To address this issue, the Agency has specified an active ingredient concentration range above the lower certified limit which may be used for efficacy testing. Active ingredient concentrations within this range [above the LCL] are considered representative of the actual lower certified limit for efficacy testing purposes. The test concentration range above the LCL is determined as follows:

1. For products with a nominal concentration less than or equal to 1.0%, the tested value for that active ingredient may be up to 2.0% above the lower certified limit stated on the CSF.

2. For products with a nominal concentration above 1.0% and less than or equal to 20.0%, the tested value for that active ingredient may be up to 1.0% above the lower certified limit stated on the CSF.

3. For products with a nominal concentration above 20.0% and less than or equal to 100.0%, the tested value for that active ingredient may be up to 0.6% above the lower certified limit stated on the CSF.

Using this approach, a product with a nominal concentration of 7.0% and a lower certified limit of 6.65% (based on 40 CFR 158.340), would have an acceptable testing range of 6.65% to 6.71%. In this example the nominal concentration is greater than 1.0% and less than 20%, therefore the allowable testing range would be up to 1.0% above 6.65% (or 6.65% to 6.71%). Products with multiple active ingredients should use this approach to determine the acceptable testing range for each active in the product.

Registrants/applicants are expected to develop formulated product samples for efficacy testing within this range. In rare cases where efforts to formulate product within this range have failed, product samples may be minimally diluted from a higher active ingredient concentration (just above the range) to achieve the target range. If product dilution is performed, a diluent that is not expected to increase product efficacy should be employed. Water is the preferred diluent in these situations. Products likely to be reactive or less stable in the presence of water may be diluted with a primary solvent already present in the product formulation. The use of emulsifiers or surfactants as diluents should be avoided even if they are already present in the subject formulation, as these may alter product efficacy. Registrants/applicants should consult with the Agency if an appropriate diluent cannot be found. Efficacy studies developed using test samples diluted with material considered likely to increase sample efficacy may be rejected by the Agency. When dilution or any other alteration is performed to achieve the acceptable LCL range, the efficacy report should specify exactly how the product was modified prior to testing.

In some cases products with reactive or unstable chemistries may be unable to achieve the allowable test range by direct formulation or by product dilution. Registrants of such products should provide a thorough justification detailing all efforts made to obtain acceptable test samples, as well as extensive rationale supporting the chemical basis for product instability. The Agency will address these situations on a case by case basis depending on the supporting information provided by the registrant, existing storage stability data for the product, and on how close the attained concentration is to the acceptable LCL range.

IV. GENERAL INFORMATION

This section is intended to summarize certain LCL testing requirements and/or specific issues which may be encountered by registrants.

- The requirement to test at the lower certified limit applies to all batches evaluated in an efficacy study and all active ingredients in the subject product.

- When efficacy testing at the LCL is performed in accordance with this notice, the inclusion of an aged batch is not required.

- As with any efficacy testing, an analytical evaluation of each batch must be performed prior to testing and the results should be included in the study report.

- Formulation changes to a registered product resulting in wider certified limits will trigger the need for efficacy testing at the new LCL.

- The use of active ingredient concentrations below the LCL for efficacy testing is permissible.

V. IMPLEMENTATION

Once this notice is finalized, applicants/registrants generating antimicrobial efficacy data for Agency submission are expected to comply with the requirements described in this notice.