

# The use of controlled hydrated diets in the context of preclinical and regulated trials made on dogs

Dominique Martel, Sylvain Tuller, SAFE, Augy, France

## Standard 326C diet and Geldiet 125C

### Synopsis

Pre-clinical animal CROs or Pharmaceutical Institutes carry out, in particular, trials with products that are still being developed. Certain products (such as ones that are anti-cancerous) may provoke problems in the way of feeding. An alternative to the standard diet-type of 'pellets' which still maintains the quality of a controlled diet is, then, deemed indispensable. The availability of new scientific data on animal testing is governed by the principles of Replacement, Reduction and Refinement, linked to the major factors influencing the animal's welfare (the '3R's').

Nutrition is one of the most important factors when it comes to the successful conduct of a pre-clinical GLP or non-GLP trial. The reduction in diet intake is often linked to the administration of a tested drug that provokes pain and/or stress in the animal, even when the standard 326C diet is rich in lipids and very appetising. It is also one of the first early warning signals, quickly followed by the appearance of severe clinical signs (a rapid loss in body weight, dehydration, etc.). This reflection stems from a study carried out on dogs with a low diet intake from the moment of first administering the trial product, such that recourse is made to a moist standard common diet, one that is not subject to controls or compliant with GLP and sourced from general distribution networks.

In the context of some types of trials on dogs, in which the administration of certain compounds leads to clear loss in appetite and entails a possible premature sacrifice made of the animals concerned, on reflection, it seemed imperative for us to remedy this lack of appetite by recourse to a hydrated and controlled diet from SAFE®, in order to avoid that premature loss of animals.

The GELDIET 125 is a complete nutritional solution, which allows you to combine the hydration and feeding of animals in one product, easily done in terms of nutritional uptake. The GELDIET 125 is made up of 73 % water and 25 % 125 dog diet.

This geldiet contributes in the way of numerous nutrients: proteins, slowly absorbed carbohydrates (starch), lipids, vitamins and minerals.

- It makes it possible to provide the main nutrients to the animals during their transportation or during a particularly difficult situation, such as post-operation convalescence,
- It can replace the standard diet,
- It is distributed in a transitory manner (for 2 to 7 days) to animals in difficult situations or in a recovery phase, as a supplement to granulated diets.

#### Characteristics of the product

Daily quantity consumed: 400-800 g/day for dogs. Daily consumption depends on the age, the sex and the condition of the animal. Method of distribution: freely or rationed, depending on the trial protocols. It is possible to maintain the classic feed (granulated 125C3, for example) available to the animals. Preservation: the product being sealed in its original packaging, can be preserved at room temperature, away from a light source, for a period of 12 months. It may be stored at 4°C

### Conclusion

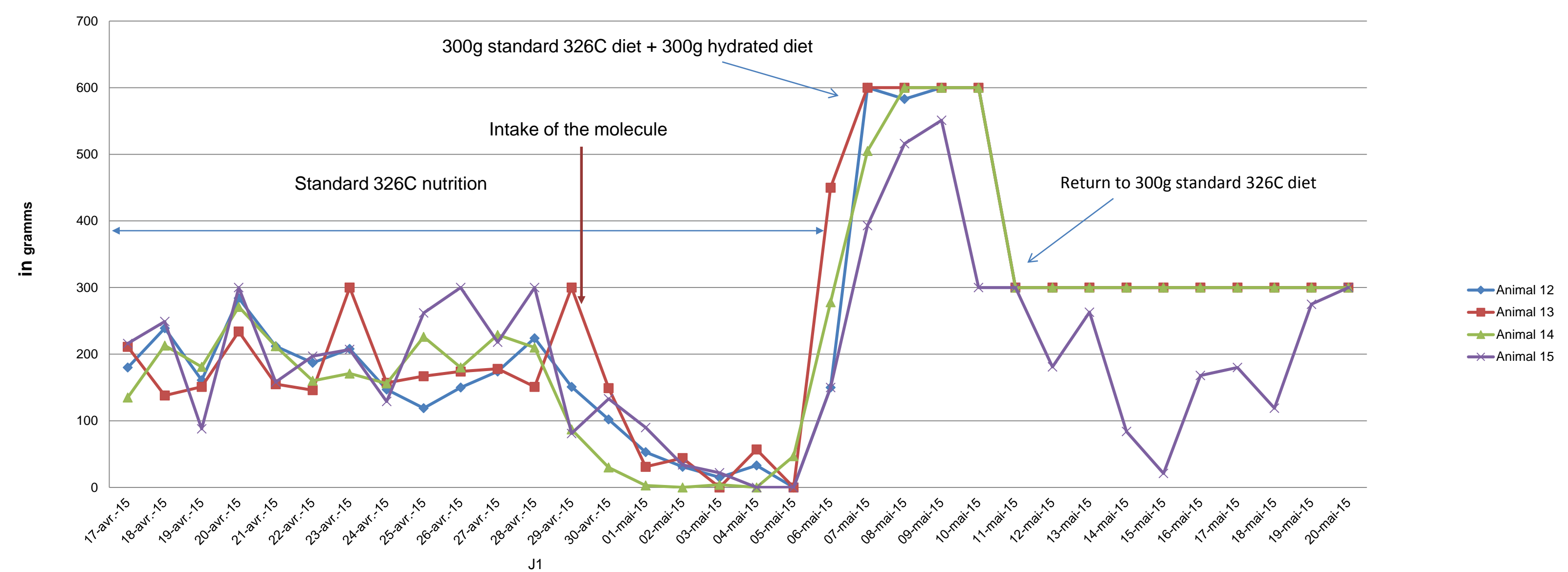
The aim of these trials was to provide an alternative to our standard diets, whilst preserving all the qualities of a controlled diet, equally to reduce the side-effects on the animal's welfare, thus meeting the requirements of the 3Rs and the GLP.

%		Geldiet 125C	326C
CARBOHYD	SUGARS	1.8	1.6
	STARCH	10.4	34.5
LIPIDS		0.9	13.0
PROTEINS		5.4	26.7
NFE	ENA	15.5	42.4
FIBER	Cellulose	0.825	2.4
ASH	cendres	1.275	6.5
MOISTURE	humidité	76.2	9.0
ME Atwater Kcal/kg		805	3522
ME Atwater MJ/kg		3.37	14.75
% ENERGIE BY LIPIDS		9.2	31.4
% ENERGIE BY PROTEIN		23.3	26.5
% ENERGIE BY NFE		67.4	42.1

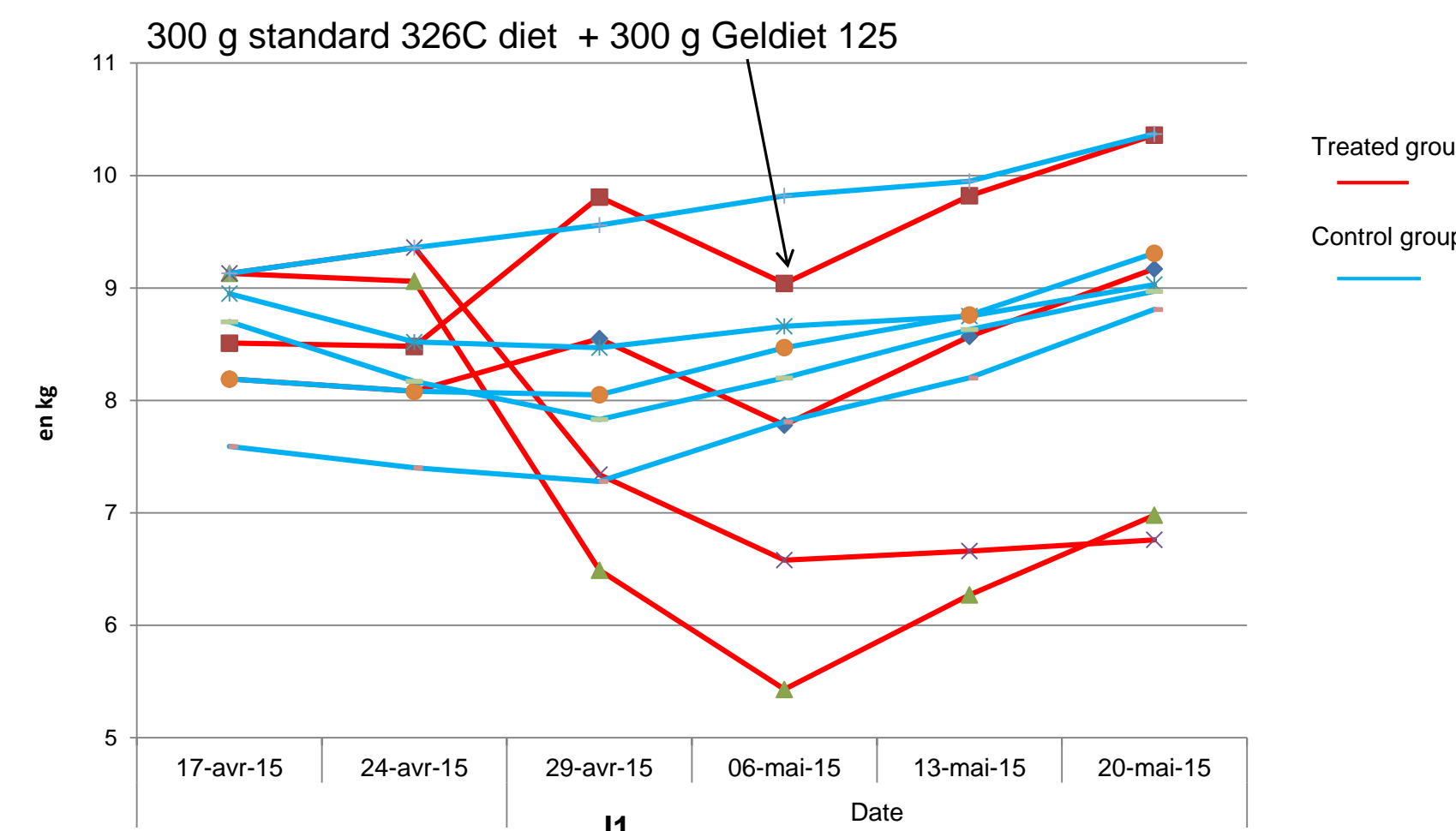
### Composition of a moist standard diet

%	Gross	Dry Matter
protein	9	44
lipids	4.5	22
Alimentary Fibers	1	9.8
minerals	2	5
Moisture	79.5	

### Food consumption



### Comparison of body weights in control and treated batches



### Male animals - Mean body weight changes expressed in kg

Dose (mg/kg/day)	Pretest Phase		Dosing Phase			
	Days 1-8	Days 1-8	Days 8-15	Days 15-22	Days 22-28	Days 28-34
0	178.3	243.8 (+36%)	300.0 (+68%)	292.4 (+63%)	265.0 (+48%)	na
20	229.0	274.3 (+19%)	300.0 (+31%)	281.6 (+23%)	287.9 (+26%)	na
60	179.5	242.8 (+35%)	287.6 (+60%)	294.6 (+65%)	250.7 (+40%)	na
180/120	182.3	97.4*** (-47%)	293.0** (+116%) <sup>1</sup>	275.3 (-5%)	289.0 (+59%)	222.2 (-22%)

Statistical analysis performed versus control group  
 \*: p ≤ 0.05 \*\* : p ≤ 0.01 \*\*\* : p ≤ 0.001  
 na: not applicable.

<sup>1</sup> Following a 5-day off dose period, animals Nos 12, 13, 14 and 15 received 300 g of hydrated food and 300 g of pellets. Animal No.14 had also received hydrated food and pellets on Days 6 and 7  
 na: Not Applicable

Values in bold: treatment-related changes  
 When compared to pretest period, compound-related body weight changes were noted in males given 180 mg/kg/day (Group 4) during the first week of dosing. They consisted in mean body weight loss of -8 % (compared to body weight gain in the control group: +4 %) associated with a marked decrease in mean food consumption (-47%).  
 These changes were associated with a low to no food intake from Day 3 (animal No.14) and were considered to be toxicologically relevant.  
 Despite hydrated food supplementation from Day 6 (for male No.14, only), 4/5 animals continued to lose weight between Day 6 and Day 8 and the decision was taken to stop the dosing for 5 days.

### Male animals - Mean food consumption per day and per period expressed in g

Dose (mg/kg/day)	Pretest Phase		Dosing Phase			
	Days 1-8	Days 1-8	Days 8-15	Days 15-22	Days 22-28	Days 28-34
0	-0.20 (-2%)	+0.35 (+4%)	+0.27 (+3%)	+0.44 (+5%)	-0.07 (-1%)	NA
20	0.06 (+1%)	+0.39 (+4%)	+0.15 (+2%)	+0.31 (+3%)	+0.10 (+1%)	NA
60	-0.15 (-2%)	+0.33 (+4%)	+0.21 (+3%)	+0.44 (+5%)	-0.07 (-1%)	NA
180/120	-0.01 (0%)	-0.63*** (-8%)	+0.55 <sup>1</sup> (+7%)	+0.50 (+6%)	+0.42*** (+5%)	+0.10 (+1%)

During the dosing period, statistical analysis was performed versus control group. Values in brackets are changes in percent as compared to pretest phase  
 \*: p ≤ 0.05 \*\* : p ≤ 0.01 \*\*\* : p ≤ 0.001  
 NA: Not Applicable

Values in bold: treatment-related changes  
<sup>1</sup>The dosing was stopped from Day 8 to day 12 included (5 days in total).  
 A compound-related decrease in food consumption (-17% compared to control group) was noted in males receiving GLP1972 at 180 mg/kg/day during the first week of the treatment. During the second week of dosing, a rebound effect in food consumption (+116% greater than pre-test values) was noted in males of Group 4 and was attributed to the 5-day off-dose period (from Day 8 to Day 12)  
 No noteworthy food consumption difference was noted in males during the two last weeks of the dosing period at 120 mg/kg/day when comparable to those observed in the control group.

### Analysis of the results

The charts given here show, at a glance, within the context of treatment once a day for 1 month, a drop in food consumption as of Day 1 of the study, linked to the administration of the product. This drop has a direct impact on the body weights. Frequently, one notices a drop in consumption on Day 1 but it is not something that should last over a period of time.

The discussion between the client, the trial manager, the veterinary, a member of the ethics committee and the technicians made it possible to undertake a swift course of action in order to re-stimulate the animals' appetite and intake.

The implementation of a ration with 300g of standard 326C diet and 300g of hydrated diet triggered an increase in food consumption as of the 1<sup>st</sup> day, with, as of the 6<sup>th</sup> May, an increase in body weights.

Four days later, the hydrated diet was withdrawn from the standard ration and three animals out of four had fully recovered, with 100% of their rations consumed. Only one animal failed to feed regularly but its weight remained stable.

### Conclusion:

The implementation of this hydrated diet allows one to maintain animals in the framework of a 'client'-sponsored trial whose product had an impact on the nutrition and thus the welfare of the animals. The hydrated diet is controlled. It is, therefore, interesting in the context of regulated trials.

### Bibliography

Nutritional care for aging cats and dogs. [Lafamme DP<sup>1</sup>. Vet Clin North Am Small Anim Pract.](#) 2012 Jul;42(4):769-91, vii. doi: 10.1016/j.cvsm.2012.04.002.

Focus on nutrition: Home-prepared diets for dogs and cats. [Weeth LP<sup>1</sup>. Compend Contin Educ Vet.](#) 2013 Mar;35(3):E3.

Evaluating pet foods: how confident are you when you recommend a commercial pet food? [Top Companion Anim Med.](#) 2008 Aug;23(3):121-6. doi: 10.1053/j.tcam.2008.04.003. [Zicker SC<sup>1</sup>.](#)

Biosafety in Microbiological and Biomedical Laboratories (BMBL)- HHS Publication No. (CDC) 21-1112

SAFE thanks Catherine Guichard, Patricia Lafouge, Damien Girault for their efficient and professional contribution to this poster