

Teklad Global Rodent Diets®

Reliable, repeatable results

Quality and scientific support

- Fixed formulation
- High-quality ingredients from approved regional suppliers
- Industry-recognized certified quality systems
- Diets designed to reduce experimental variability





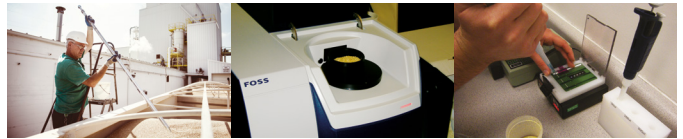
Quality processes drive consistency

Fixed formula diets contain the **same ingredients, in the exact same quantities, in every batch of diet.**

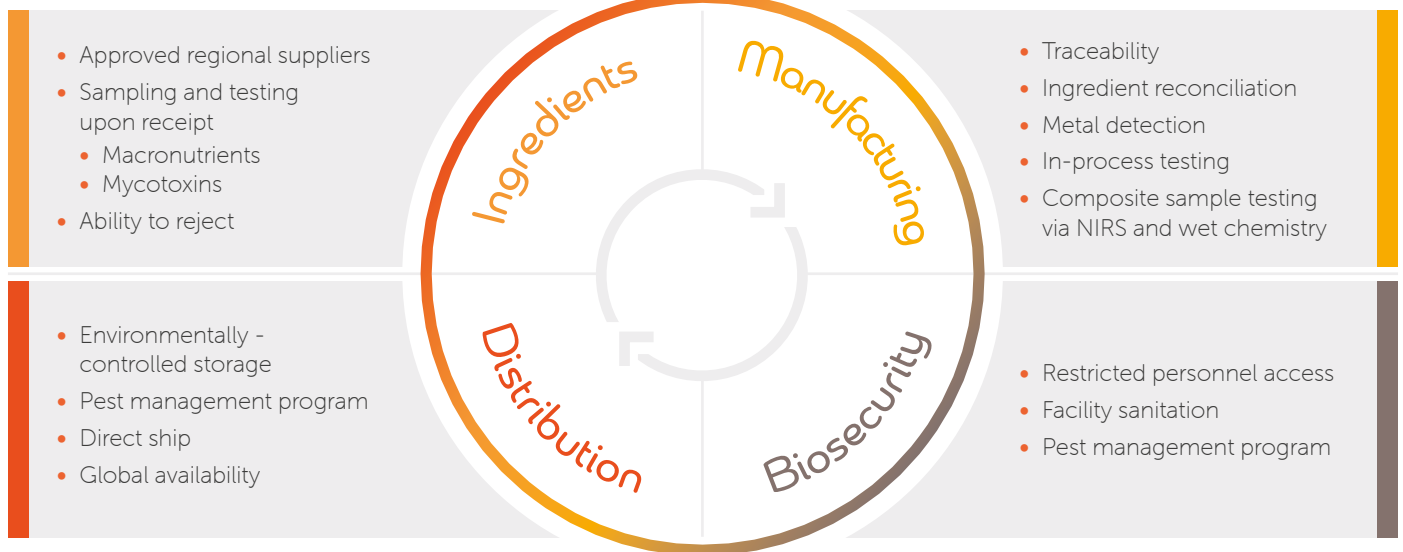
- Diet is a critical variable in any study
- Our fixed formulation philosophy and quality practices translate to consistent research results for you
- Other manufacturers may use variable formula diets in which both ingredients and inclusion rates are changed to an extent unknown to the investigator

TEKLAD DIETS: A FIXED FORMULATION APPROACH

Method	Ingredients from approved suppliers are tested prior to acceptance and use.
Rationale	Both nutrients and non-nutrients can have important effects.
Result	Minimize nutrient variation and manage non-nutrient variation while maintaining formula integrity.



Bulk ingredients are sampled across the depth and length of the load and tested for macronutrients and mycotoxins





Teklad Global Rodent Diets

A RELATED FAMILY OF DIETS FOR SPECIFIC LIFE STAGES AND RESEARCH PURPOSES

TEKLAD GLOBAL RODENT DIETS					
DIET	2014	2016	2018	2019	2020X
Primary ingredients (Order of inclusion)	Wheat midds Wheat Corn Corn gluten meal Soy oil	Wheat Corn Wheat midds Corn gluten meal Soy oil	Wheat Corn Wheat midds Soybean meal Corn gluten meal Soy oil	Wheat Corn Corn gluten meal Wheat midds Soy oil	Wheat Corn Corn gluten meal Wheat midds Soy oil
CALCULATED NUTRIENT PROFILE (AS FORMULATED)					
Protein %	14.3	16.4	18.6	19.0	19.1
Fat %	4.0	4.0	6.2	9.0	6.5
Metabolizable energy	2.9 kcal/g 12.1 kJ/g	3.0 kcal/g 12.6 kJ/g	3.1 kcal/g 13.0 kJ/g	3.3 kcal/g 13.8 kJ/g	3.1 kcal/g 13.0 kJ/g
Isoflavone content*	<20 mg/kg	<20 mg/kg	150-340 mg/kg	<20 mg/kg	<20 mg/kg
USE AND FEATURES					
Life stage	Long-term maintenance	Growth, maintenance	Breeding, growth	Breeding, higher energy	Breeding, growth
Purpose and benefits	<ul style="list-style-type: none"> • Prolonged maintenance • Aging • Toxicology • Oncology 	<ul style="list-style-type: none"> • Growth • Maintenance • Toxicology • Oncology 	<ul style="list-style-type: none"> • Breeding • Growth • Maintenance • General purpose 	<ul style="list-style-type: none"> • Breeding • Genetically - engineered mice • Poorly performing strains • Oncology 	<ul style="list-style-type: none"> • Breeding • General purpose • Estrogen-sensitive breeding studies • Reproductive toxicology • Oncology

* Expected range of genistein + daidzein (aglycone) based on quarterly measurement of diet

TEKLAD GLOBAL RODENT DIETS – DESIGNED TO REDUCE EXPERIMENTAL VARIABILITY

- Modern formulations
- Levels of protein, energy, vitamins and minerals more closely align with nutritional requirements
- Reduce or eliminate **soybean meal**, and exclude alfalfa meal, the major sources of phytoestrogens in rodent diets
- Vegetarian diets eliminate nitrosamines as a research variable
- Available globally to promote protocol consistency

VARIATIONS IN PRODUCT CODE NOMENCLATURE

- '9' in the second digit - the diet has been irradiated
- 'S' - the autoclavable version, supplemented with vitamins to account for presumed losses
- 'X' - extruded form; exception is 2019 which is extruded
- 'C' - certified; a representative sample is tested for a panel of contaminants
- 'M' - meal form

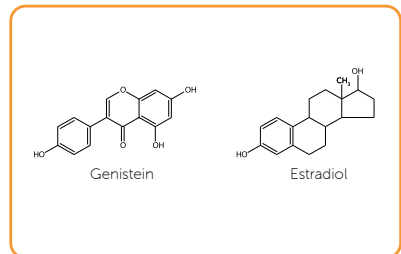
Not all product combinations are produced regularly or stocked locally.



Ingredient selection

THE KEY TO REDUCING RATHER THAN INTRODUCING VARIATION

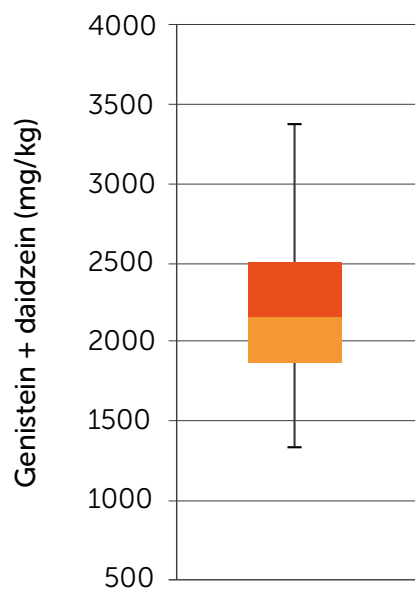
INGREDIENT	COMPONENT	SIGNIFICANCE
Soybean meal	Isoflavones: Genistein, Daidzein	Selective Estrogen Receptor Modulator
Alfalfa meal	Coumestrol	Selective Estrogen Receptor Modulator
	Chlorophyll	Interferes with fluorescent imaging
Fish meal, Meat meal	Nitrosamines	Potential carcinogen



- These ingredients of concern have been reduced or eliminated in the Teklad Global Rodent Diets.
- To learn how diet impacts research results, see examples that follow.

ISOFLAVONE LEVELS IN SOYBEAN MEAL WILL VARY MORE THAN TWO-FOLD OVER TIME

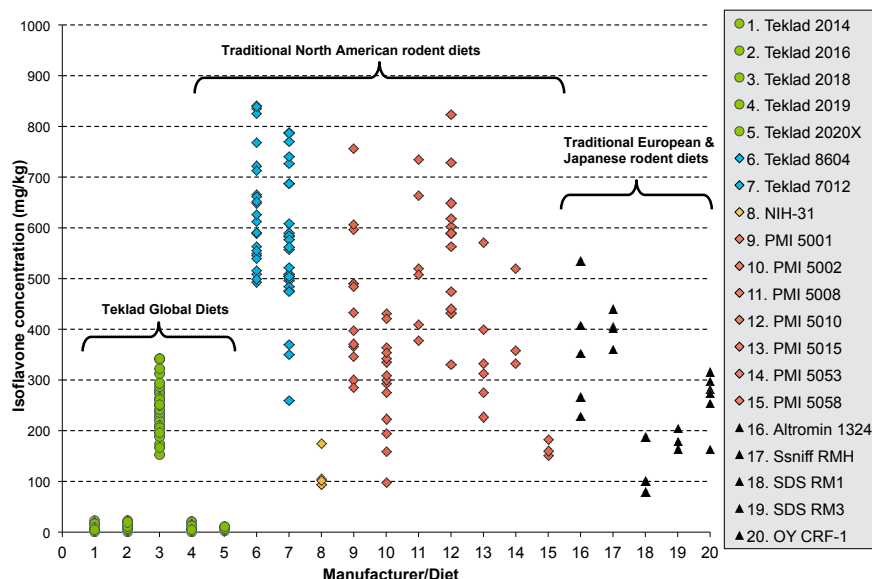
- Soybean meal is the primary source of phytoestrogens in rodent diets, containing the isoflavones genistein and daidzein.
- Plot at right shows distribution of isoflavone content in soybean meal sourced by Envigo from 2003–2015 (n=51; expressed as aglycone form).
- Variability is primarily due to growing location and conditions.
- Within year variability is minimized by regional sourcing; between year variability accounts for the wide range in soybean meal isoflavone levels.





VARIATION IN ISOFLAVONE LEVELS (GENISTEIN + DAIDZEIN) BETWEEN DIETS AND WITHIN BATCHES OF THE SAME DIET

Plot shows isoflavone levels for traditional diets from North America (blue, yellow, red), Europe and Japan (black) and Teklad Global Rodent Diets (green). Data is compiled from published literature and commercial laboratory analysis. Each symbol is one value; symbols within a column denote multiple values for that diet.



For experimental endpoints sensitive to isoflavones, batch-to-batch variation can lead to inconsistency, confounding your interpretation of results.

KEY PRINCIPLES

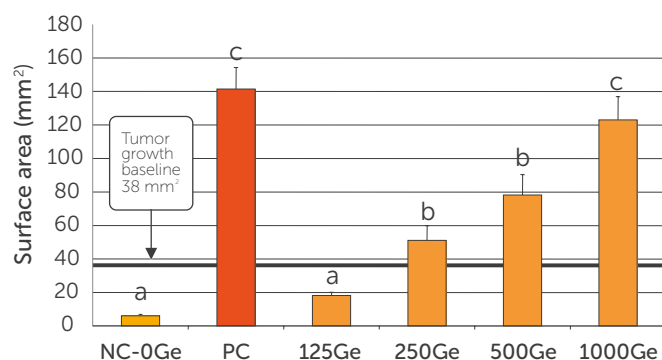
- Isoflavone range in rodent diets that contain soybean meal is 100-700 mg/kg.
- Estrogen receptors (ER) are widely distributed in tissues.
- Isoflavones have considerable access to ER by virtue of high serum levels.

WAYS IN WHICH ISOFLAVONES IMPACT RESEARCH

RESEARCH AREA	EFFECTS DESCRIBED IN THE LITERATURE
Oncology	Modulate tumor growth, latency, multiplicity, metastasis; diminish action of drugs such as tamoxifen and letrozole.
Reproductive	Increase uterine weight; accelerate vaginal opening; affect response to exogenous estrogens/xenobiotics.
Endocrine	Differences in body composition (weight, adiposity), glucose and insulin homeostasis, bone density, and blood pressure.
Neuroscience	Performance differences on tests measuring anxiety behaviors and response to pain stimuli.
Immunology	Modulate immune organ development; display anti-inflammatory and antioxidant actions.



TUMOR GROWTH IN MICE CONSUMING VARIOUS LEVELS OF GENISTEIN AT 22 WEEKS AFTER REMOVAL OF ESTROGEN PELLET



NC = AIN-93G // PC = E17b
 Ju YH, et al. 2001. Physiological concentrations of dietary genistein dose-dependently stimulate growth of estrogen-dependent human breast cancer (MCF-7) tumors implanted in athymic nude mice. *J Nutr* 131:2957-2962

ESTROGEN-DEPENDENT MAMMARY TUMORS RESPOND TO DIETARY GENISTEIN

Model

- OVX athymic BALB/c mouse

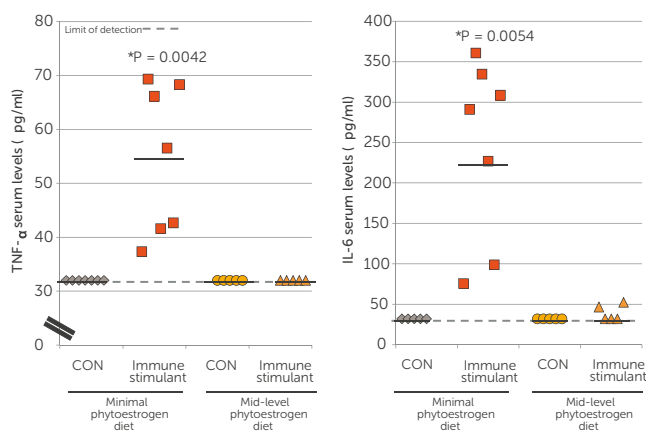
Treatments

- Implanted with estrogen pellet and MCF-7 cells
- E pellet removed at 38 mm²
- Mice fed purified diet AIN-93G with genistein (0, 125, 500, or 1000 ppm) for 22 weeks

Results

- Genistein in diet stimulated growth of estrogen-dependent MCF-7 cells in dose dependent fashion

CYTOKINE LEVELS IN MICE AFTER EXPOSURE TO VIRAL STIMULANT AND SWIM STRESS



Vasiadi et al, (2014) Isoflavones inhibit poly(I:C)-induced serum, brain, and skin inflammatory mediators - relevance to chronic fatigue syndrome. *J. Neuroinflammation* 11:168.

MINIMAL ISOFLAVONE DIETS RESULT IN A MORE ROBUST RESPONSE TO IMMUNOLOGICAL CHALLENGE

Model

- Female C57BL/6 mouse model of chronic fatigue syndrome (CFS)

Treatments

- Natural ingredient diets with or without soybean meal
- Saline or the viral simulant Poly(I:C) with swim stress

Results

- Feeding a diet without soybean meal led to a significant immune response.
- Animals fed minimal phytoestrogen diets recapitulated CFS phenotype.

CHALLENGE: ISOFLAVONES IMPACT RESEARCH

- No simple absolute threshold for the physiological effects of phytoestrogens
- Difficult to predict magnitude and direction of response
- Their action reduces effectiveness of animal model
- Preclinical research in rodent models fed diets containing soybean meal may not translate to human populations due to differences in consumption levels and metabolism

Solution: Inotiv's minimal isoflavone Teklad diets lead to reliable, repeatable research results.

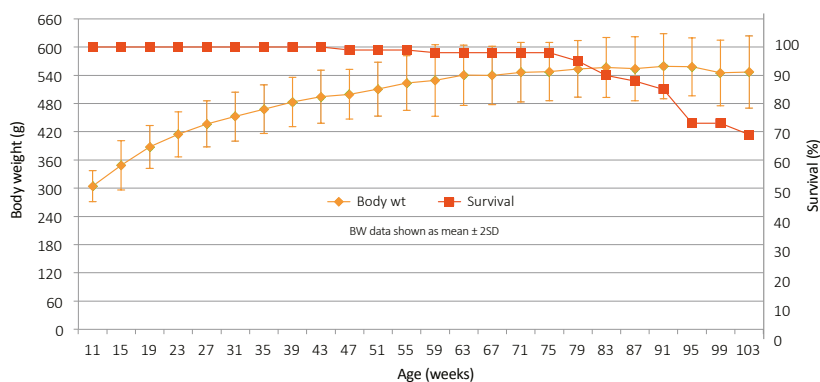


Teklad Global Rodent Diets

DESIGNED TO IMPROVE ANIMAL WELFARE

- Other commonly used diets supply protein well in excess of requirements and can contribute to early mortality
- There are benefits to lower protein, lower energy standard diets for toxicology and safety studies

GROWTH AND SURVIVAL CURVES



Model

Hsd:Sprague Dawley®
SD® males (n=200)

Diet

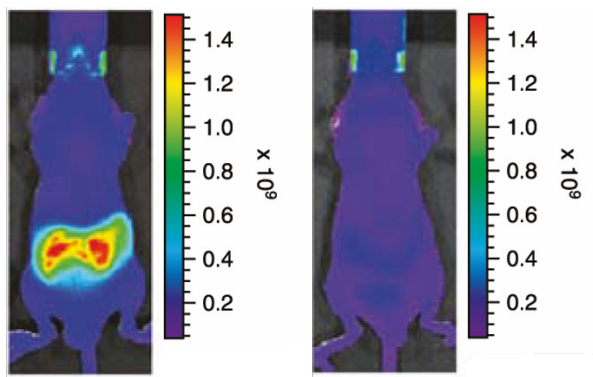
Teklad 2014 (14% protein)
starting at 8 weeks of age

Results

- Body weight plateaus at ~550 grams without diet restriction; compare to CD® IGS rat which are 100-200 grams heavier when fed more typical standard diets
- Survival at 2 years ~68%; compare to typical 2 year survival in CD® IGS rat of ~35-40%

Teklad Global Rodent Diets

FOR FLUORESCENT IMAGING



- Exclusion of alfalfa meal practically eliminates chlorophyll, the source of autofluorescence in the gut region
- Teklad Global Rodent Diets significantly reduce background autofluorescence and are suitable for many imaging applications



Inotiv Teklad Products

Reliable, repeatable results

Known for superior customer service, technical expertise, and sales support.

CUSTOM RESEARCH DIETS

Control nutrients

- Vitamin or mineral adjusted
- Protein or amino acid adjusted
- Lipid or fatty acid adjusted

Induce disease

- Atherogenic (cholesterol, fat, cholate)
- Diet-induced obesity (40–60% fat kcal)
- High carbohydrate (fructose, sucrose)
- NaCl adjusted
- Cuprizone demyelination

Dose animals

- Control of gene expression – doxycycline or tamoxifen containing diets
- Addition of customer-supplied ingredients/compounds

STANDARD NATURAL INGREDIENT DIETS FOR MULTIPLE SPECIES

- Global
- Traditional

BEDDING AND ENRICHMENT

- Contact
- Non-contact

MEDICATED DIETS

- Fenbendazole
- Ivermectin
- Uniprim

Complimentary consultation
with our nutritionists – contact
askanutritionist@inotivco.com