

The SAFE Letter

NEWSLETTERS



The needs and requirements of the research world are changing at an increasing speed. So we at SAFE are focused on responding quickly to your needs and on guaranteeing you a consistent offer over time.

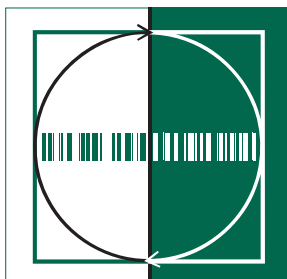
This has motivated us to hold workshops events in several cities. These discussions are an opportunity for us to come together to speak about current issues. We will be continuing these events this year with new topics.

Like every year, we have chosen to focus on a particular aspect of laboratory animal nutrition. Here, we have provided a scientific overview of several of the nutritional aspects of particular importance during the sensitive reproductive phase.

The SAFE team is pleased to welcome Jean-Jacques Haltel as plant manager. You will find his illustration of the latest improvement initiatives that have been implemented. After 4 years at SAFE, Eric Thouvenin has also had the opportunity to take on new responsibilities within the group, and we would like to thank him for his contribution.

I and the entire SAFE team hope that you will enjoy this newsletter and wish you the very best for the new year 2012. May it be a year full of confidence for you and your teams in which all of your projects come into being.

Georges HASSON,
General Manager
For SAFE Team



Medicated Diets

SAFE's special diet preparation unit is ANSES certified, the essential regulatory prerequisite for the production of medicated diets. This unit's design and independence uphold SAFE's commitments: high-quality products, zero cross contamination, well-controlled processes and traceability. This is where we produce our standard, irradiated or autoclavable diets for curative or preventive parasite treatments. SAFE can provide you with precise information on this topic. .



SAFE AND THE ENVIRONMENT

More efficient waste sorting

By obtaining ISO 14001 certificate, we at SAFE have documented our drive to control our environmental impact to the best of our ability. Toward this aim, we have implemented a selective sorting system. Under the system, one bin is set aside for organic waste, which is then composted by a specialised facility, and the second bin is reserved for other waste, which is then sorted at a certified outside location.



DIETS AND BREEDING

Breeding situations depend primarily on animals' gene pool, as well as on the breeding system which determines the potential for gene expression. Diet can be used to determine a phenotype based on the previous parameters. The effects of diet are not limited to the animal; rather, they also impact its environment and that of the operator.

The challenges

Diet has a crucial impact on rodents' lives. Indeed, an animal is often fed the same diet throughout its entire life. Anyone involved in reproduction is aware that animals' fertility, prolificity, growth and general state of health are also controlled by diet. A diet is determined by its analytical composition as well as by its palatability, consumption, digestibility, toxicological and sanitary quality, and more. As a result, these parameters can be adapted in order to optimise the performances of a strain.

The needs of a reproducing animal vary considerably in both quantity and quality during the different stages of development. Meeting these changing needs over time is a way to optimise breeding performances, particularly for the most sensitive animals and transgenic strains.

For example, in mice, Vitamin E is crucial to placenta development. As a result, it is important to supply sufficient quantities between the 6th and the 14th day after mating for this species (Jishage et al., 2005).

An increasing number of studies are demonstrating the effect of diet at early stages in utero and even multi-generational effects (Cooney, 2006). When reproducing female mice in the oocyte maturation phase are fed with a maintenance phase diet, cardiac

IMPACT OF DIET

ANIMALS	ENVIRONMENT	OPERATOR
Covers nutritional needs depending on stage of development	Enrichment of the environment	Easiness to handle
Digestive health, prevention of digestion related pathologies	Nitrogen emissions	Reduced waste
Control of contaminations	Litter quality (quantity of urine and faeces)	Litters' cleanliness

and behavioural anomalies appear in the young. These anomalies are not observed when the mothers are fed with diet with the appropriate protein content for their physiological stage (Watkins et al., 2008).

While nutritional factors must be controlled, these are not the only factors with an important role in diets. Indeed, diets include substances liable to induce physiological or even pathological effects. This is why certain heavy metals, pesticides, mycotoxins, endocrine disruptors and nitrosamines are regulated. Certain standards partially determine the maximum and acceptable doses most appropriate to research. (GV-SOLAS-BARQA-EPA). However, there is no such thing as zero risk.

Compliance with these doses does not guarantee the total absence of contaminants. Effective risk management requires higher standards and the implementation of best practices starting in the field and throughout the transport, storage and transformation of all raw materials. Only the selection of those raw materials with the lowest possible levels of contaminants and

SAFE IS SAFE-R

A new record room

In order to meet your requirements for end-to-end traceability, we have built a new Archives facility with input/output control and reinforced fire protection.

Along with the record room, we use a safe in order to better protect our computer back-ups..

EVEN SAFE-R PRODUCTS

A renovated sample bank

At SAFE, we store vacuum samples of all of our finished products and ingredients for a period of 2 years. We have set aside a special sample facility in order to boost traceability and transparency.

J.H



well-controlled processes can procure less-contaminated diets.

While nutritional solutions can meet each need, they make colonies more complex to manage and complicate work in the animal facility. This is undoubtedly why the most common choice for breeding is a system based on a single diet.

Non-diet-related factors and challenges in breeding performances have changed considerably over time. While diet can constitute a non-negligible potential for improvement, it has not yet been thoroughly explored with regard to the thousands of existing strains. A better balance can be struck between animal facilities' constraints and animals' needs.

SAFE has developed diets for each physiological stage, single diets appropriate for all stages, other diets that are appropriate for transgenic, weakened, or post-operative animals, and more.

SAFE puts its expertise to work to meet your specific requirements. We can develop tailored solutions for your research. Contact us!

Some of the possible physiological effects of nutrition on reproductive parameters.

NUTRIENT	EFFECTS ON REPRODUCTION
Proteins and Amino acids	Passive immunity in newborns from milk. Growth, milk production, etc.
Energy	Influences animals' overall performances: growth, reproduction, etc. Deficiency: causes cannibalism Reduction: increases life expectancy, reduces weight problems and tumour development.
Lipids	Excess: obesity reduces fertility in mice (Tortoriello et al. 2004) and reduces sperm mobility in rats (Fernandez et al., 2011)
Omega 3 and 6 unsaturated fatty acids	Involved in prostaglandin synthesis. Influence mammary gland development
Vitamin A	Cancer-fighting agent in embryonic development (Olson, 2001). Deficiency: sterility. On young: depend on mother's milk and dietary regimen upon weaning (very low vitamin A levels in the liver)
Vitamin E (α-tocopherol)	Deficiency: severely lowers reproductive performances (Ames, 1974).
Vitamin B12 (cobalamine)	Deficiency: causes retarded growth and renal atrophy in rats
Vitamin B9 (Acide folique)	Deficiency: slows growth and lowers reproductive capacities
Vitamin D	Deficient rats: adding calcium and phosphorus improves performances (Uhland et al., 1992) Deficiency: causes rachitis.
Vitamin B1 (Thiamine)	Deficiency: testicle degeneration
Trace elements	Bioavailability differs by chemical form. Deficiency : often leads to retarded growth
Iron	Deficiency during gestation: causes retarded growth in the young (Lewis et al.,2001,2002)
Phytoestrogens	Endocrine disruptors (Thigpen et al. 2004)
Antioxidants	Inhibits the development of ovarian theca cells and causes apoptosis (Rzeczynska et al., 2011).

NEWS FLASH

ZEBRAFISH, NUTRITIONAL INNOVATION

Following an in-depth study of the zebrafish's nutritional needs and the new models that have been developed, SAFE introduces the new, zebrafish-specific CAVIAR range.

CAVIAR offers

- Classification of the agglomerated product in a wide range of sizes to match all of the stages of development,
- Smallest diameter between 5 and 50µm, for

consumption from the very first days, and the possibility to substitute for Artemia and paramecia,

- High-quality raw materials with excellent bioavailability and a low level of contaminants,
- Specific micro-encapsulation technology in partnership with a unit specialising in young fish nutrition.

The technical information is available by request or on our website, www.safe-diets.com



DID YOU KNOW?

All packaging that comes into contact with diet must be food grade certified. All of SAFE's packaging that comes into contact with your products has this certification. The certificates are available upon your request.

Welcome to the new Hungarian distributor INNOVO Kft. SAFE thus expands its distribution level.



WORKSHOPS

We are continuing to hold round table discussions in various cities in France. Workshops are also planned abroad.

Our aim is to discuss a variety of topics: Dietary contaminants, Biofilm, Nutrition, and more. The success with which these topics were met when presented at various Afstal workshops has encouraged us to continue this initiative.

You will be receiving an invitation including all of the details for each SAFE round table event.

G.M



LOGIQUAL

At SAFE, as you are aware, our formulas remain identical and the origin of our ingredients as well as our processes are unchanged and well-controlled. However, due to the extensive data we have collected, improvements of analytical methods and the increasingly precise searches that are performed, we have needed to invest in a more powerful and flexible software solution: **LOGIQUAL**.

This system allows us to compile all of the analytic data on our finished products (diets and litters) as well as on our raw materials).

LOGIQUAL will provide a more complete presentation of our control data sheets and allow graphs and raw data to be extracted. Through LOGIQUAL, SAFE provides you with a secure, durable solution with which to manage all analytic data.

We have so updated our analytic data as well as our products' technical information. Those product data sheets have also changed shapes, **but SAFE's formulas remain identical.**

R.B & D.M

Route de Saint Bris - 89290 Augy - France
Tél. :+33 (0)3 86 53 76 90 - Fax : +33 (0)3 86 53 35 96 - info@safe.evls.net

WWW.SAFE-DIETS.COM

Cooney, 2006. Germ cells carry the epigenetic benefits of grandmother's diet. PNAS. 103 : 17071–17072. •

Cropley et al., 2006. Germ-line epigenetic modification of the murine Avy allele by nutritional supplementation. PNAS. 103 : 17308–1731 • EPA, US Environmental Protection Agency, <http://www.epa.gov/> • Fernandez et al., 2011. Diet-induced obesity in rats leads to a decrease in sperm motility. Reproductive Biology and Endocrinology, 9:32 doi:10.1186/1477-7827-9-32 • GV-SOLAS, Gesellschaft für Versuchstierkunde, <http://www.gv-solas.de/> •

Jishage et al., 2005. Vitamin E Is Essential for Mouse Placentation but Not for Embryonic Development Itself. Biology of Reproduction November 1, vol. 73 no. 5 983-987 • Olson JA - Handbook of vitamins, 2001 • Tortoriello et al., 2004. Dietary-Induced Obesity and Hypothalamic Infertility in Female DBA/2J Mice. Endocrinology, vol. 145 no. 3 1238-1247 • Watkins et al., 2008. Low protein diet fed exclusively during mouse oocyte maturation leads to behavioural and cardiovascular abnormalities in offspring. J Physiol 586 : 2231–2244 • Ames, 1974. Age, parity, and vitamin A supplementation and the vitamin E requirement of female rats. American Journal of Clinical Nutrition, Vol 27, 1017-1025 • Uhland et al., 1992. Normalization of serum calcium restores fertility in vitamin D-deficient male rats. J Nutr. Jun; 122(6):1338-44 • Lewis et al., 2002. Long-term programming of blood pressure by maternal dietary iron restriction in the rat. British Journal of Nutrition, 88, 283–290 • Lewis et al., 2001, 2002. Effects of maternal iron restriction in the rat on blood pressure, glucose tolerance, and serum lipids in the 3-month-old offspring. Metabolism: Clinical and Experimental, 50, (5), 562-567 • Thigpen et al. 2007. Variations in Phytoestrogen Content between Different Mill Dates of the Same Diet Produces Significant Differences in the Time of Vaginal Opening in CD-1 Mice and F344 Rats but Not in CD Sprague-Dawley Rats. Environ Health Perspect. December; 115(12): 1717–1726 • Rzepczynska et al., 2010. Antioxidants induce apoptosis of rat ovarian theca-interstitial cells. Biology of Reproduction September 15, 2010 • www.safe-diets.com