

**HLAL RDNA CONSTRUCT IN SBC LAL-C CHICKENS- hlal rdna construct in sbc
lal-c chicken not applicable
Alexion Pharmaceuticals, Inc.**

hLAL rDNA Construct in SBC LAL-C Chickens

Heritable construct

1. PRODUCT IDENTIFICATION

hLAL rDNA construct integrated at a single site (the SYN LAL-C site in chromosome 6) as a single copy, in a specific, diploid line (SBC LAL-C¹) of hemizygous and homozygous domestic chickens (*Gallus gallus*) derived from the lineage progenitor XLL 109, expressing a recombinant human lysosomal acid lipase (rhLAL) encoding gene such that rhLAL protein (intended for the treatment of humans) is present in their egg whites.

1 SBC LAL-C is the name Alexion designated for their lineage of chickens, and is not representative of the regulated article, which is subject to FDA approval. The FDA-regulated article subject to this approval is the intentional genomic alteration (hLAL rDNA construct) in the chickens.

2. WARNINGS AND PRECAUTIONS

SBC LAL-C chickens, or any materials derived from them, are not intended to enter the human or animal food supply.

3. ANIMAL SAFETY

Data from the following comparisons of SBC LAL-C chickens to comparator chickens (without an intentional genomic alteration; IGA) demonstrated a lack of adverse effect due to the rDNA construct, or to the recombinant human LAL protein, on the SBC LAL-C chicken.

Mortality rates² for SBC LAL-C chickens and comparators without an IGA housed under similar conditions are presented in **Table 1**. These data include mortality rates collected at multiple Alexion animal facilities housing multiple generations of SBC LAL-C chickens collected during 2015 to 2017.

Table 1: Historical Mortality Results for SBC LAL-C Hens (Measured by Age)

Hen Age (weeks)	21-25	26-30	31-35	36-40	41-45	46-50	51-55	56-60	61-65	66-70	71-75	76-80
Average Weekly Mortality Rate*	0.05%	0.10%	0.22%	0.17%	0.21%	0.19%	0.26%	0.39%	0.38%	0.37%	0.38%	0.74%
Standard Deviation	0.12%	0.19%	0.30%	0.28%	0.32%	0.32%	0.32%	0.42%	0.46%	0.44%	0.47%	1.34%
Comparator Hens†	0%	0.13%	0.20%	0.48%	0.07%	0.07%	0.58%	0.23%	0.17%	N/A	N/A	N/A

* Based on data from 19 populations, years 2015 through 2017

† Comparator chickens (hens) are those without an intentional genomic alteration

In a study to compare physiological endpoints SBC LAL-C vs. comparator chickens without an IGA, blood samples were collected for serological assays, and chickens were presented for post-mortem examination for gross/histological evaluations. No differences between LAL-C chickens and comparators without an IGA were evident based on the following evaluations: serology and histopathology, including CBC (complete blood count), comprehensive blood chemistry, triglycerides and LDH (lactate dehydrogenase) and histopathological examination of multiple tissues.

SBC LAL-C hens produced eggs over a 3-year period at the same average annual rate as comparator hens without an IGA housed under similar conditions (**Table 2**).

These values are also consistent with the 280 eggs per hen produced per year reported for White Leghorn flocks in commercial egg production facilities³.

Table 2:Egg Production Rates for LAL-C Chickens and Comparators without an Intentional Genomic Alteration

Hen Age (weeks)	25	30	35	40	45	50	55	60	65	70
SBC LAL-C Hens:										
Average*	28.9	58.4	87.4	116.2	145.9	174.4	201.6	224.2	247.5	272.1
Standard Deviation	4.3	4.3	5.3	6.3	7.7	8.7	9.8	11.3	13.7	14.7
Comparator Hens†										
Average	31	63	93	118	147	173	198	222	248	274

* Based on data from eight production rooms at two production facilities

† Comparator chickens (hens) are those without an intentional genomic alteration

The data for SBC LAL-C chickens versus comparator chickens without an IGA demonstrates no significant differences in, mortality, general health status or egg production.

2 Mortality as attributed to animal death and euthanasia for items such as broken legs/wings, cloacal prolapse or other injury.

3 Austic, R. E., Nesheim, M. C. Poultry production, 1990, Lea & Febiger, Philadelphia, US

4. EFFECTIVENESS

Multiple generations of the SBC LAL-C line have demonstrated genetic consistency as established through genetic tests for the presence of the hLAL rDNA construct, hLAL rDNA DNA sequence fidelity and hLAL rDNA construct integration site consistency. For each generation, phenotypic consistency has been established based on the presence of recombinant human LAL enzyme activity in egg white.

5. LIMITATIONS OF USE

The SBC LAL-C lineage must be housed in only those Alexion Pharmaceutical, Inc. facilities specified in the approved application.

Manufactured by:

Alexion Pharmaceuticals, Inc.

121 Seaport Boulevard,

Boston, MA 02210.

Approved by FDA under NADA #141-453

[version 002/2020]

November/2020

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Product Information			
Product Type	RECOMBINANT DEOXYRIBONUCLEIC ACID CONSTRUCT LABEL	Item Code (Source)	NDC:25682-020
Route of Administration	NOT APPLICABLE		

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
HLAL RDNA CONSTRUCT IN SBC LAL-C CHICKEN (UNII: MG6AU4C2HB) (HLAL RDNA CONSTRUCT IN SBC LAL-C CHICKEN - UNII:MG6AU4C2HB)	HLAL RDNA CONSTRUCT IN SBC LAL-C CHICKEN	1 [arb'U] in 1 [arb'U]

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:25682-020-01	1 [arb'U] in 1 NOT APPLICABLE		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
NADA	NADA141453	12/08/2015	

Labeler - Alexion Pharmaceuticals, Inc. (789359510)

Revised: 6/2021

Alexion Pharmaceuticals, Inc.