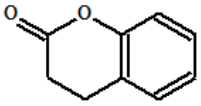
Dihydrocoumarin

CAS N°:	119-84-6	**Empirical formula:** **Structure:**	$C_9H_8O_2$ 
Synonyms:	1,2-Benzodihydropyrone 2H-1-Benzopyran-2-one, 3,4-dihydro- Chroman-2-one 2-Chromanone 3,4-Dihydro-2H-1-benzopyran-2-one o-Hydroxydihydrocinnamic acid lactone Melilotic acid lactone		

History:	Initial reviews:	October 1974	
	Current revision date:	June 2013	
	Implementation date:	For new submissions*:	August 10, 2013
		For existing fragrance compounds*:	August 10, 2014
	Next review date	2018	

* This date applies to the supply of fragrance compounds (formulas) only, not to the finished products in the marketplace.

RECOMMENDATION:	**RESTRICTED**

RESTRICTIONS:

Limits in the finished product:			
Category 1 See Note box (1)	0.029%	Category 7	0.08 %
Category 2	0.037 %	Category 8	1.01 %
Category 3	0.15 %	Category 9	5 %
Category 4	0.45 %	Category 10	2.5 %
Category 5	0.24 %	Category 11	See Note box (2)
Category 6	0.72 %		

Note box:

(1) IFRA would recommend that any material used to impart perfume or flavour in products intended for human ingestion should consist of ingredients that are in compliance with appropriate regulations for foods and food flavourings in the countries of planned distribution and, where these are lacking, with the recommendations laid down in the Code of Practice of IOFI (International Organisation of the Flavor Industry - www.iofiorg.org)
(2) Category 11 includes all non-skin contact or incidental skin contact products. Due to the negligible skin contact from these types of products there is no justification for a restriction of the concentration of this fragrance ingredient in the finished product.

Fragrance material specifications:	N/A

CONTRIBUTION FROM OTHER SOURCES:

See **Annex I**

Dihydrocoumarin

CRITICAL EFFECT:	SENSITIZATION

RIFM SUMMARIES:

LLNA weighted mean EC3 values ($\mu g/cm^2$) [no. studies]	Potency Classification Based on Animal Data[1]	Human Data			WoE NESIL[3] ($\mu g/cm^2$)
		NOEL – HRIPT (induction) ($\mu g/cm^2$)	NOEL – HMT (induction) ($\mu g/cm^2$)	LOEL[2] (induction) ($\mu g/cm^2$)	
1070 [3][4]	Moderate	NA[5]	NA	2000	1000

All data in this Table are available from RIFM and are listed in the RIFM Database.
NOEL = No observed effect level; HRIPT = Human Repeat Insult Patch Test; HMT = Human Maximization Test; LOEL = lowest observed effect level; NA = Not Available.

[1]Based on animal data using classification defined in ECETOC, Technical Report No. 87, 2003.
[2]Data derived from HRIPT or HMT.
[3]WoE NESIL limited to two significant figures.
[4]EC3 value from the mean of the individual LLNAs.
[5] An HRIPT conducted on 49 subjects produced 2 questionable reactions which were not confirmed.

REXPAN RATIONALE / CONCLUSION:

The RIFM Expert Panel reviewed the critical effect data for Dihydrocoumarin and, based on the weight of evidence, established the No Expected Sensitization Induction Level (NESIL) as 1000 $\mu g/cm^2$, which is a default value based on the LLNA data. They recommend the limits for the 11 different product categories, which are the acceptable use levels of Dihydrocoumarin in the various product categories. These were derived from the application of the exposure-based quantitative risk assessment approach for fragrance ingredients, which is detailed in the publication by Api *et al*., 2008.

REFERENCES:

Api AM, Basketter DA, Cadby PA, Cano M-F, Ellis G, Gerberick GF, et al, 2008. Dermal Sensitization Quantitative Risk Assessment (QRA) For Fragrance Ingredients. *Regulatory Toxicology and Pharmacology* 52(1): 3-23.

Kimber, I., Hilton, J., Weisenberger, C., 1989. The murine local lymph node assay for identification of contact allergens: A preliminary evaluation of in situ measurement of lymphocyte proliferation. *Contact Dermatitis*, 21, 215-220.

Kimber, I., Weisenberger, C., 1991. Anamnestic responses to contact allergens: Application in the murine local lymph node assay. *Journal of Applied Toxicology*, 11(2), 129-133.

Opdyke, D.L.J. (1974), *Food and Cosmetics Toxicology* 12, 521.

RIFM (Research Institute for Fragrance Materials, Inc.), 2003. Evaluation of skin sensitization potential of coumarin in mice using the Local Lymph Node Assay (LLNA). Unpublished study from Rhodia, Inc. Report number 47072. (RIFM, Woodcliff Lake, NJ, USA).

RIFM (Research Institute for Fragrance Materials, Inc.), 2012. Local Lymph Node Assay on Dihydrocoumarin. Draft RIFM report number 63816. (RIFM, Woodcliff Lake, NJ, USA).