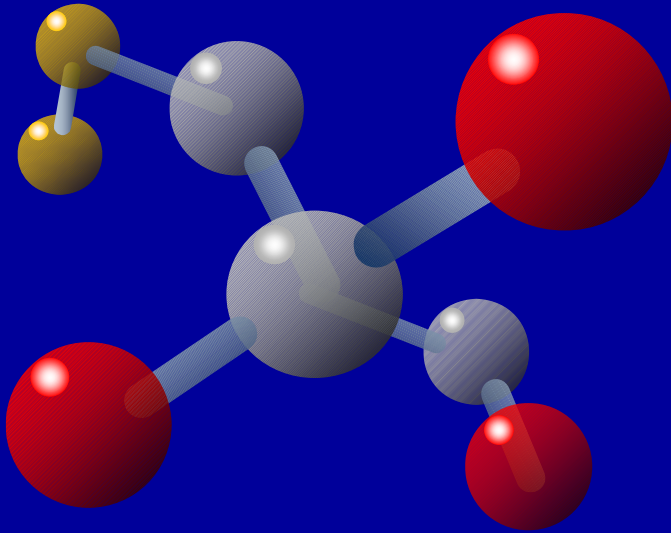


# Allergy vaccines: the importance of the active principle

more important than the pharmaceutical form,  
either tablets, drops or injections!

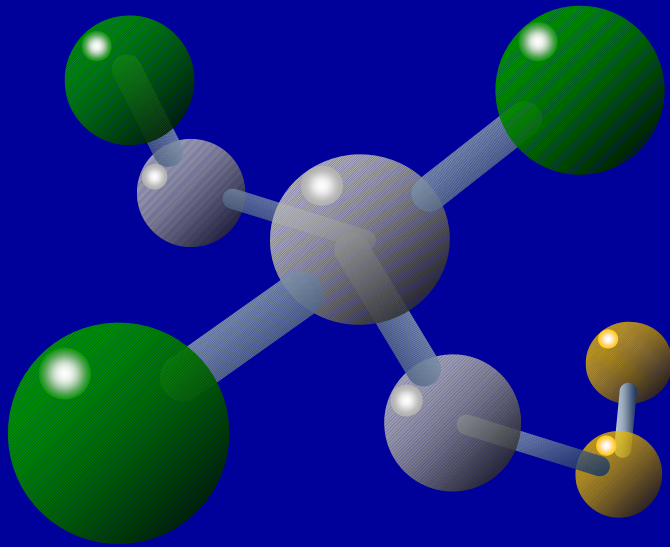
*LOFARMA S.p.A.*  
*2010*

# The Allergen



This is a simplification of an **allergen** molecule, for example of a weed.

# The Carbamylated Allergoid

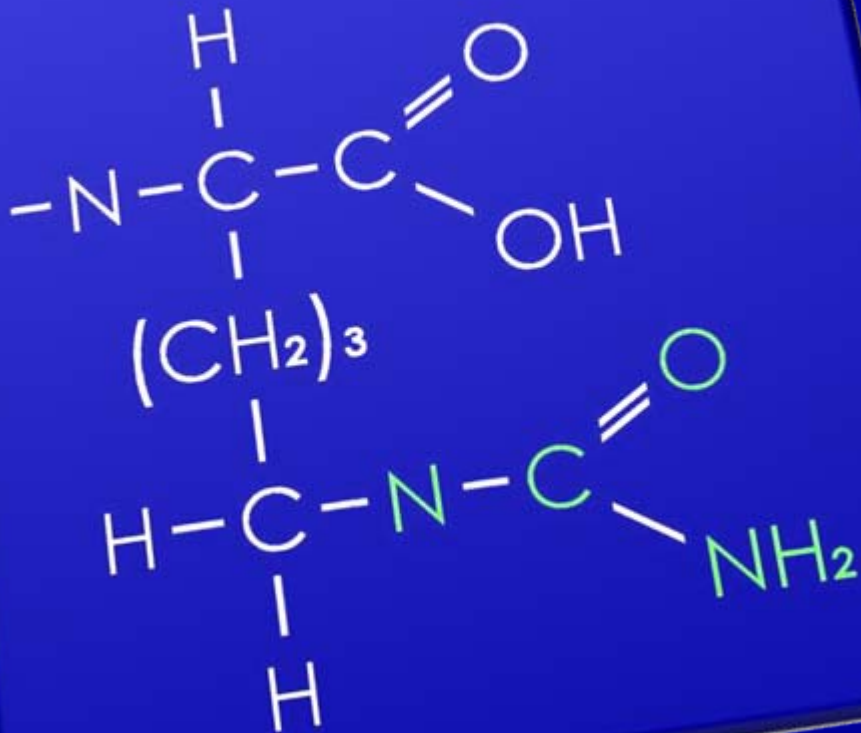


This is a simplification of an **allergoid** molecule, a chemical modification of an **allergen**.

The Carbamylated Allergoid is obtained by carbamylation with potassium cyanate at alkaline pH, a reaction that leads to a substantial substitution of the allergen lysine aminogroups: a **well-definite** active principle.

# what are the consequences ?

Carbamylated Allergoid



1

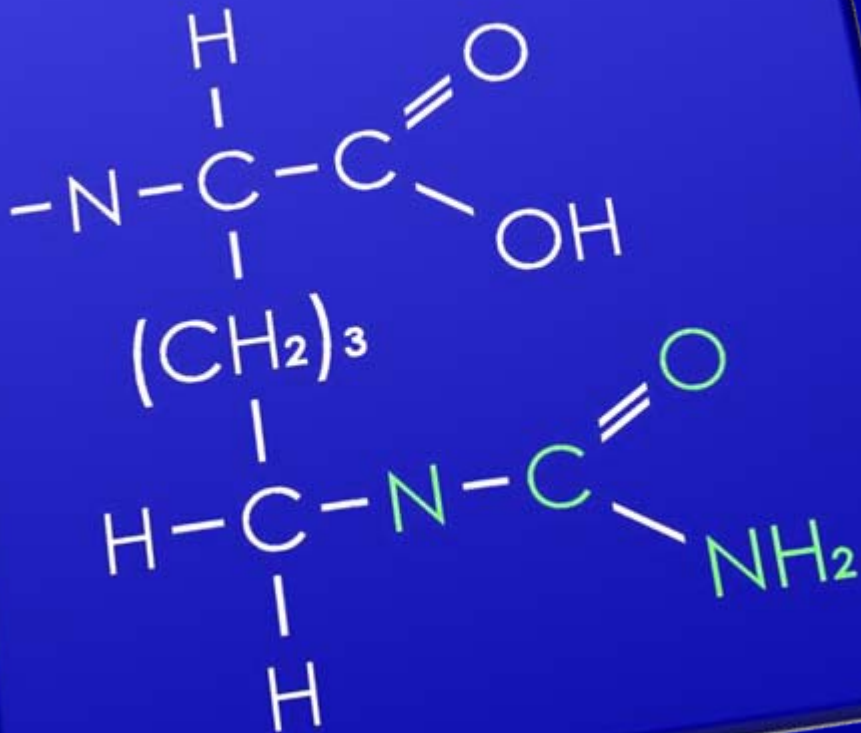
Dramatic reduction  
of specific IgE linking

reduced  
allergenic activity

SAFETY

# what are the consequences ?

Carbamylated Allergoid



2

Resistance to enzymatic degradation

carbamylated allergoid  
remains active

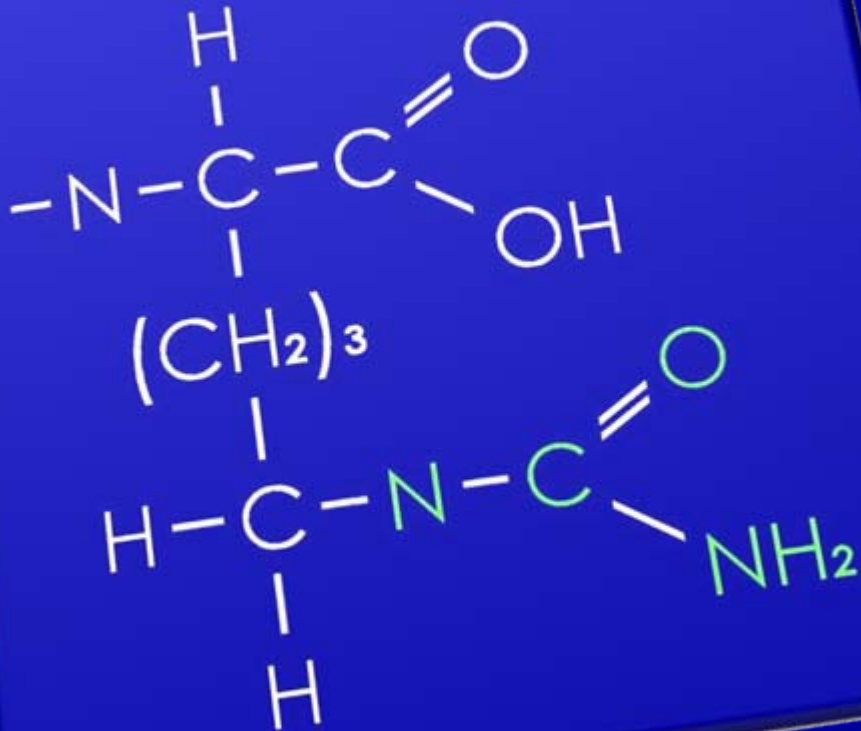


*"high doses"* are not necessary.

**EFFECTIVE DOSES**

# what are the consequences ?

Carbamylated Allergoid



3

NO  
alteration of T-epitopes

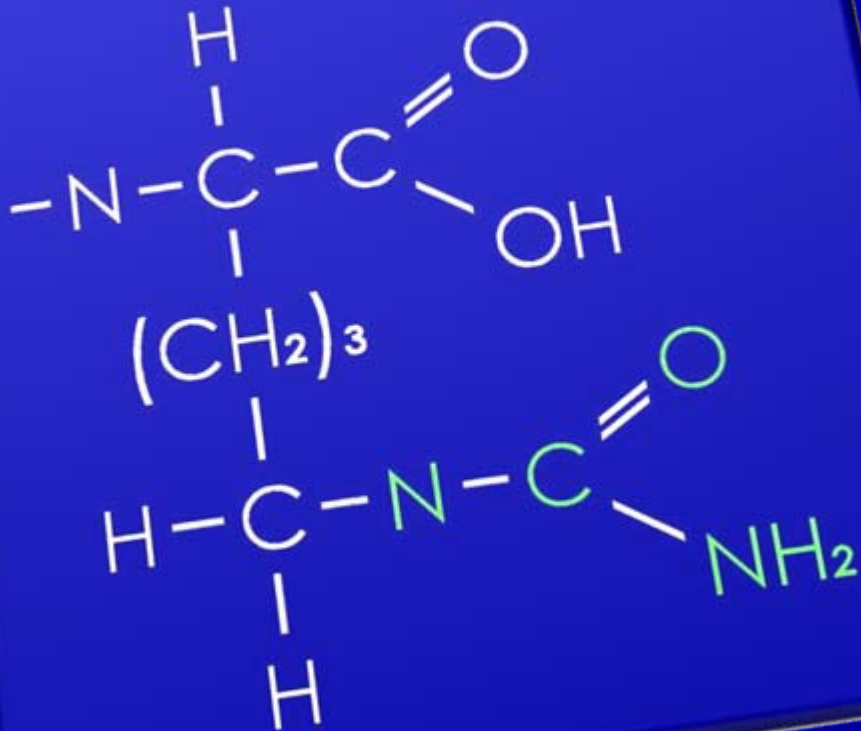
preserved  
immunogenic activity



EFFICACY

# what are the consequences ?

Carbamylated Allergoid



4

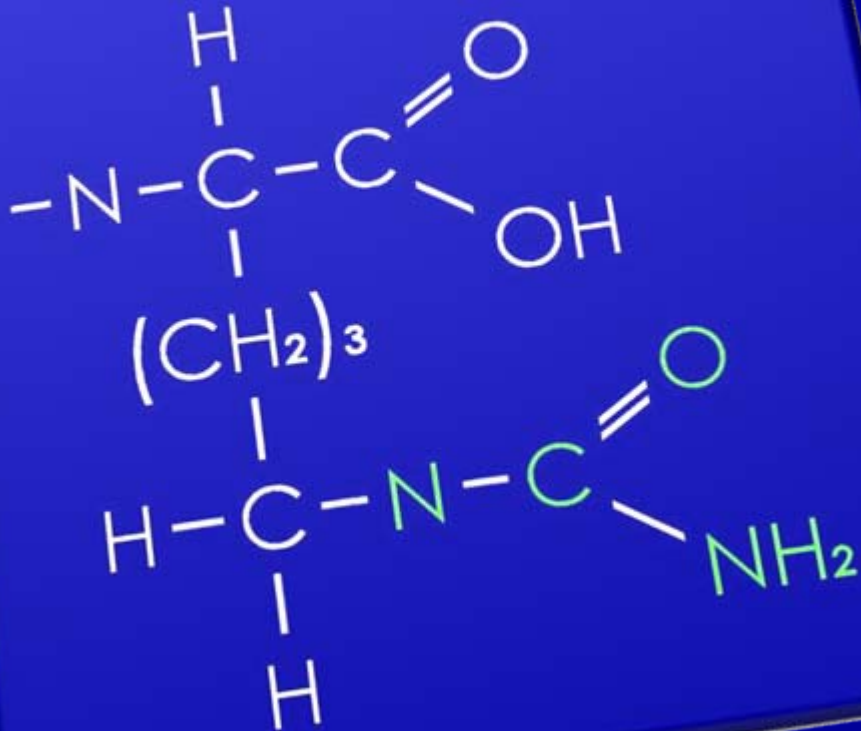
**PRESERVATION**  
of molecular sizes

Carbamylated Allergoid is  
a Monomeric Allergoid

**FIT for SLIT**

# what are the consequences ?

Carbamylated Allergoid



5

**IRREVERSIBILITY**  
of carbamylation

NO back to  
native allergen



**SAFETY**



# selected references

## Synopsis of published Lais studies

## Part 1: study design

AUTHOR	JOURNAL	Study	Adults/Children	No. Patients	Diseases*	Allergen	Treatment	Tablets/Drops
Bordignon	Giorn It Allergol Immunol Clin 1994;4:153-159	DBPC	adults, children	60	OR and/or A	Grass	preseasonal	Tab
Pacor	Rec Prog Med 1996;87(1):4-6	open	adults	34	OR	Grass	preseasonal	Tab
Caffarelli	Allergy 2000;55:1142-7	DBPC	children	48 (24A+24P)	R, C or A	Grass	preseasonal	Tab
Lombardi	J Invest Allergol Clin Immunol 2001; 11:41-45	open	adults	51 (26A+25C)	RC and/or A	Grass	preseasonal	Tab
Palma-Carlos	Allergol Immunopathol 2006;34(5):194-198	DBPC	adults	33	R with or without A	Grass	preseasonal	Tab
Burastero	Ann All Ast Imm 2006;100:343-350	open	adults	11	R	Grass	preseasonal	Tab
Pacor	Rec Prog Med 1995;86(12):489-91	open	adults	14	A	Mites	continuous	Tab
La Rosa	Not Allergol 1996;15:45-46	open	children	30	A and/or RC	Mites	continuous	Tab
Passalacqua	The Lancet 1996;351:829-32	DBPC	adults	20 (10A+10P)	RC	Mites	continuous	Tab
Marogna	Int Journ Imm Pharm 2001;14:93-101	observational (SLIT, SIT, intranasal)	adults	29 A + 12 C (SLIT)	OR with or without A	Mites	continuous	Tab
Passalacqua	Allergy 2006;61:849-854	DBPC	adults	56 (A+ P)	R	Mites	continuous	Tab
Cosmi	Clin Exp All 2006;36:261-292	open	adults	25 (A+C)	R with or without A	Mites	continuous	Tab
Ippoliti	Pediatr Allergy Immunol 2006;17:337-345	open	children	40	A	Mites	continuous	Drops
Marogna	Int Arc All Imm 2007;142:70-78	retrospective	adults	65 (53 A+12C)	R	Mites	continuous	Tab
Marogna	Eur Ann Allergy Clin Immunol 2008;40:22-29	retrospective	adults	101 (57 A+44C)	R	Mites	continuous	Tab
Ariano	Invest Allergol Clin Immunol 1996;8(3):155-160	DBPC	adults	30 (15A+15P)	R with or without A	Parietaria	pre-co-seasonal	Tab
D'Anneo	Allergol Immunopathol 2008;36(2):79-84	open	adults	65 (24A+21A+21C)	R and/or A	Parietaria	co-seasonal	Tab
Lombardi	Allergy 2001;56:989-992	open (safety)	adults	198	R and/or A	Mites(20), Grass(75), Olive(1), birch(4), Parietaria(35)	preseasonal or continuous	Tab
Marogna	Eur Ann All Imm Clin 2003;35(4):133-140	observational (SLIT, SIT, intranasal)	adults, children	106 A (Lais)+ 170 C	R and A	Mites(44), Grass(98), birch(2)	continuous	Tab
Rossi	Giorn It Allergol Immunol Clin 2002; 12: 221-228	open (safety)	adults	13	R and/or A	Grass + Mites	-	Tab
Arena	Int Journ Imm Pharm 2003;16:277-282	open	adults	60	R with or without A	Mites(20), Grass(5), Olive(2), Parietaria(24)	preseasonal or continuous	Tab
Agostinis	Allergy 2005;60:133	open (safety)	children	36	A or R	Mites, Grass	continuous	Drops
Gammeri	Allergol Immunopathol 2005;33(3):142-4	open (safety)	adults, children	105 (28 c+77a)	R or A	Mites(56), Grass(15), Parietaria(34)	-	Tab
Rossi	Int J Immunopathol Pharmacol 2005;16:277-285	open (safety)	adults	45	RC and/or A	Grass + Mites	-	Tab
Giordano	Eur Ann All Imm Clin 2006;38(9):310-312	open	adults	39	R with or without A	Mites(27), Grass(7), Olive(3), Cat(1), Parietaria(1)	continuous	Tab
La Grutta	Eur Ann Clin Immunol 2007;39:40-44	open	adults/children	56 (33A+ 23C)	A with or without R	Mites + Parietaria	continuous	Tab
Burastero	Int J Immunopathol Pharmacol 2009; 22:343-352	open	adults	11	R	Birch	pre-co-seasonal	Tab
Mezei	Not Allergol 1996;15:40-44	DBPC	adults/children	60 (30A+30Chie) 20A+10P in each group	RC with or without A	Ragweed	pre-co-seasonal	Tab
Ariano	Eur Ann All Imm Clin 2005;37(3):103-108	open	adults	30 (20A+10C)	RC and/or A	Cypress	pre-co-seasonal	Drops
Rolla	EAACI 2009	open	adults	21	RC and/or A	Birch	pre-co-seasonal	Tab

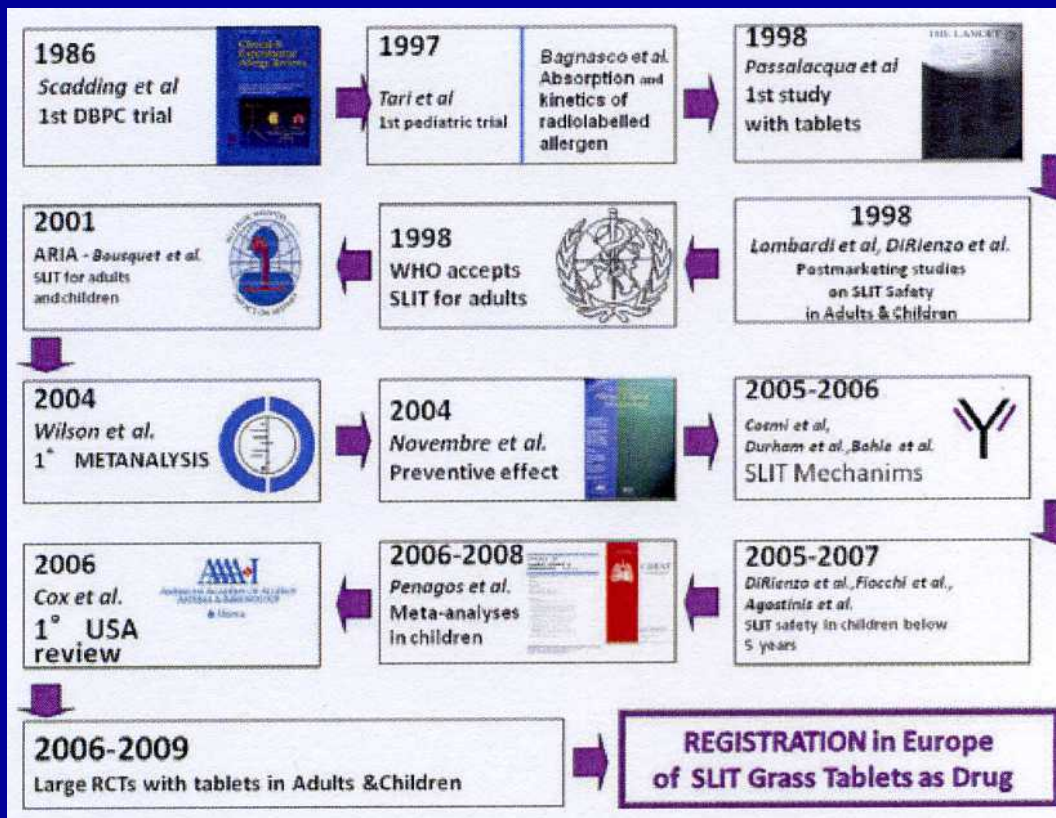
OR = Oculo-Rhinitis; A = Asthma; C = Conjunctivitis; RC = Rhino-Conjunctivitis

## Synopsis of published Lais studies

## Part 2: results

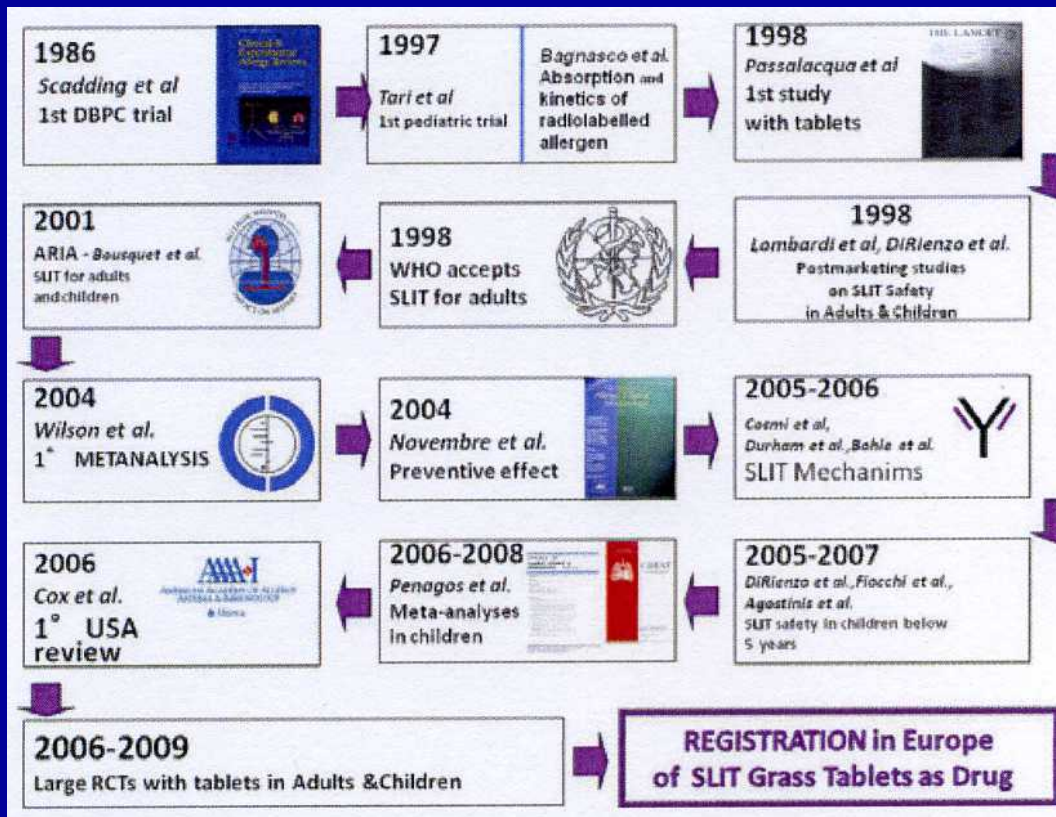
AUTHOR	JOURNAL	Treatment		Results Symptoms	Results Drugs	Results Mch	Cumulative dosages in AU/year
		Build up	Maintenance AU				
Bordignon	Giorn It Allergol Immunol Clin 1994;4:153-159	14 weeks	1000/week	reduction	reduction	-	36,500
Pacor	Rec Prog Med 1996;87(1):4-6	14 weeks	1000/week	reduction	reduction	-	36,500
Caffarelli	Allergy 2000;55:1142-7	7 weeks	3000/week	reduction	=	-	37,250
Lombardi	J Invest Allergol Clin Immunol 2001; 11:41-45	14 weeks	-	reduction	reduction	reduction bronch. reac.	36,000
Palma-Carlos	Allergol Immunopathol 2006;34(5):194-198	14 weeks	2000/week	reduction	reduction	reduction nasal reac.	40,500
Burastero	Ann All Ast Imm 2006;100:343-350	-	14000/week	-	-	-	120,000
Pacor	Rec Prog Med 1995;86(12):489-91	14 weeks	1000/week	reduction	-	reduction	62,500
La Rosa	Not Allergol 1996;15:45-46	3 weeks	300/week	reduction	reduction	-	23,775
Passalacqua	The Lancet 1996;351:829-32	14 weeks	4000/week	reduction	reduction	reduction CMAI, ECP	176,500
Marogna	Int Journ Imm Pharm 2001;14:93-101	14 weeks	2000/week	reduction	reduction	reduction bronch. reac.	100,000
Passalacqua	Allergy 2006;61:849-854	4 weeks	2000/week	reduction	reduction	quality of life improvement	116,000
Gosmi	Clin Exp All 2006;36:261-292	8 weeks	1000/week	reduction	-	immunological eval. (L-10)	60,000
Ippoliti	Pediatr Allergy Immunol 2006;17:337-345	4 weeks	1800/week	reduction	-	reduction bronch. reac.	43,950
Marogna	Int Arc All Imm 2007;142:70-78	14 weeks	1000/week	reduction	-	reduction bronch. reac.	62,500 (1 year) 218,500 (4 years)
Marogna	Eur Ann Allergy Clin Immunol 2008;40:22-29	14 weeks	1000/week	reduction	-	reduction bronch. reac.	62,500
Ariano	Invest Allergol Clin Immunol 1996;8(3):155-160	14 weeks	2000/week	reduction	reduction	reduction nasal reac.	72,525
D'Anneo	Allergol Immunopathol 2008;36(2):79-84	3 days	1000 or 3000/week	reduction (VAS)	reduction	reduction bronch. reac.	32,000 or 84,000
Lombardi	Allergy 2001;56:989-992	8 weeks	2000/week	-	-	-	20,850 or 104,800
Marogna	Eur Ann All Imm Clin 2003;35(4):133-140	14 weeks	1000/week	reduction	reduction	reduction bronch. reac.	62,500
Rossi	Giorn It Allergol Immunol Clin 2002; 12: 221-228	2 hours	2000/week	-	-	-	-
Arena	Int J Immunopathol Pharmacol 2003;16:277-282	14 weeks	4000/week	reduction	reduction	-	176,500
Agostinis	Allergy 2005;60:133	3 weeks	4200/week	reduction	-	-	216,000
Gammeri	Allergol Immunopathol 2005;33(3):142-4	20 minutes	2000/week	-	-	-	-
Rossi	Int J Immunopathol Pharmacol 2005;16:277-285	20 minutes	2000/week	-	-	-	-
Giordano	Eur Ann All Imm Clin 2006;38(9):310-312	4 days	2000/week	reduction (VAS)	reduction	-	108,000
La Grutta	Eur Ann Clin Immunol 2007;39:40-44	16 days	2000/week	reduction	reduction	reduction bronch. reac.	110,000
Burastero	Int J Immunopathol Pharmacol 2009;22:343-352	-	15,000/month	reduction	reduction	immunological eval. (L-10)	90,000
Mezei	Not Allergol 1996;15:40-44	8 weeks	2000 5 week 1000 9 week	reduction	reduction	reduction nasal reac. signific. in ad.	33300
Ariano	Eur Ann All Imm Clin 2005;37(3):103-108	16 days	900/week	reduction	reduction	reduction nasal reac.	22,900
Rolla	EAACI 2009	-	6000/week or 2000/week	reduction	reduction	-	120,000 or 208,000
Fancello	EAACI 2008	4 days	1000/week	reduction (VAS)	-	-	57,000

# The contribution of carbamylated allergoid in the history of SLIT



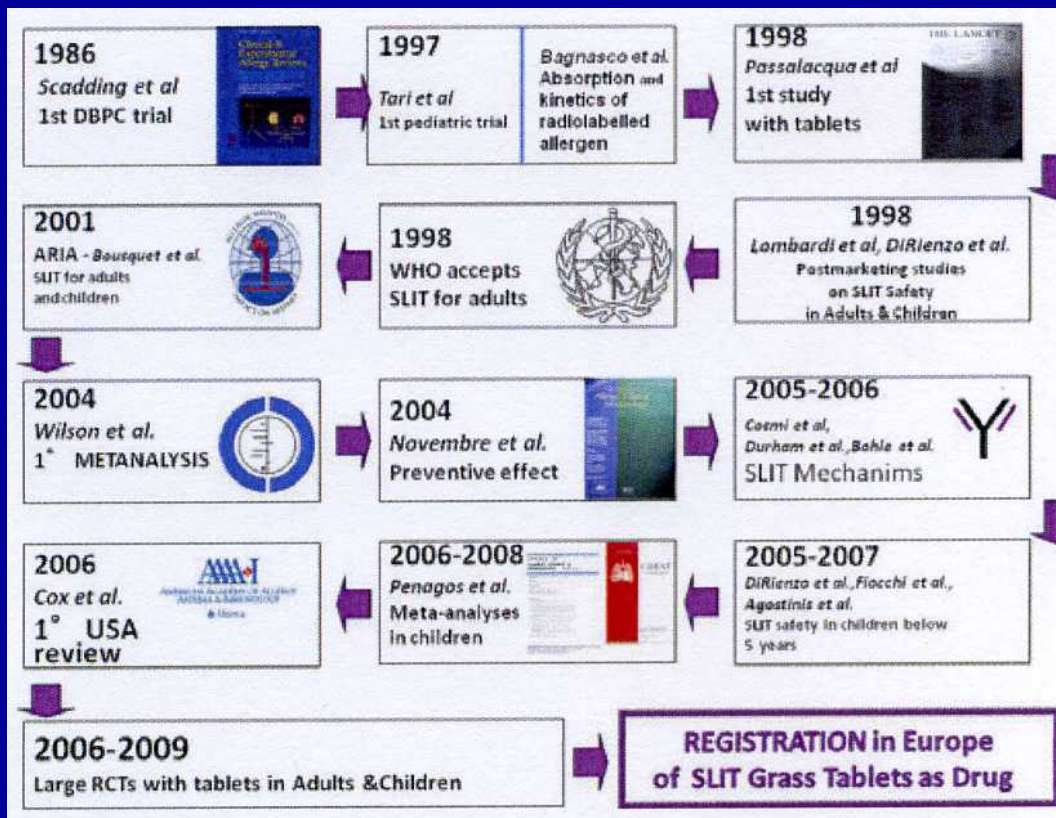
1997  
Bagnasco, JACI  
1<sup>o</sup> study on kinetics

# The contribution of carbamylated allergoid in the history of SLIT



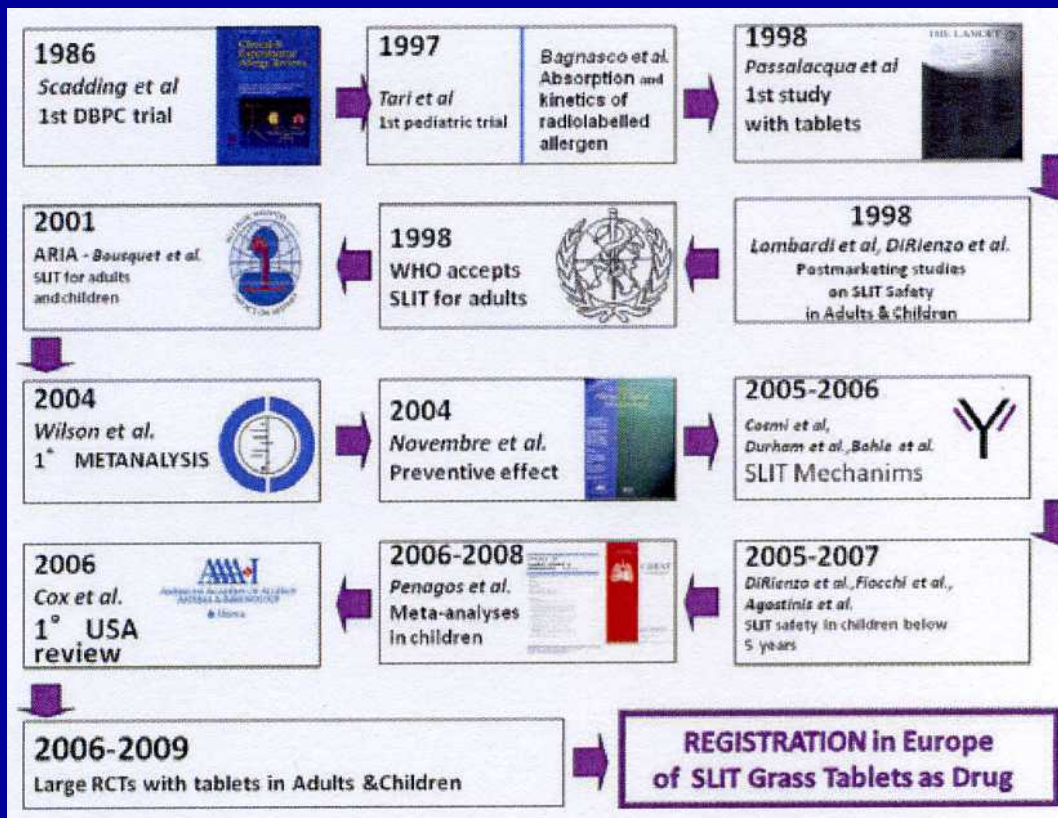
1998  
Passalacqua, Lancet  
1<sup>o</sup> study with  
tablets,  
allergoid tablets

# The contribution of carbamylated allergoid in the history of SLIT



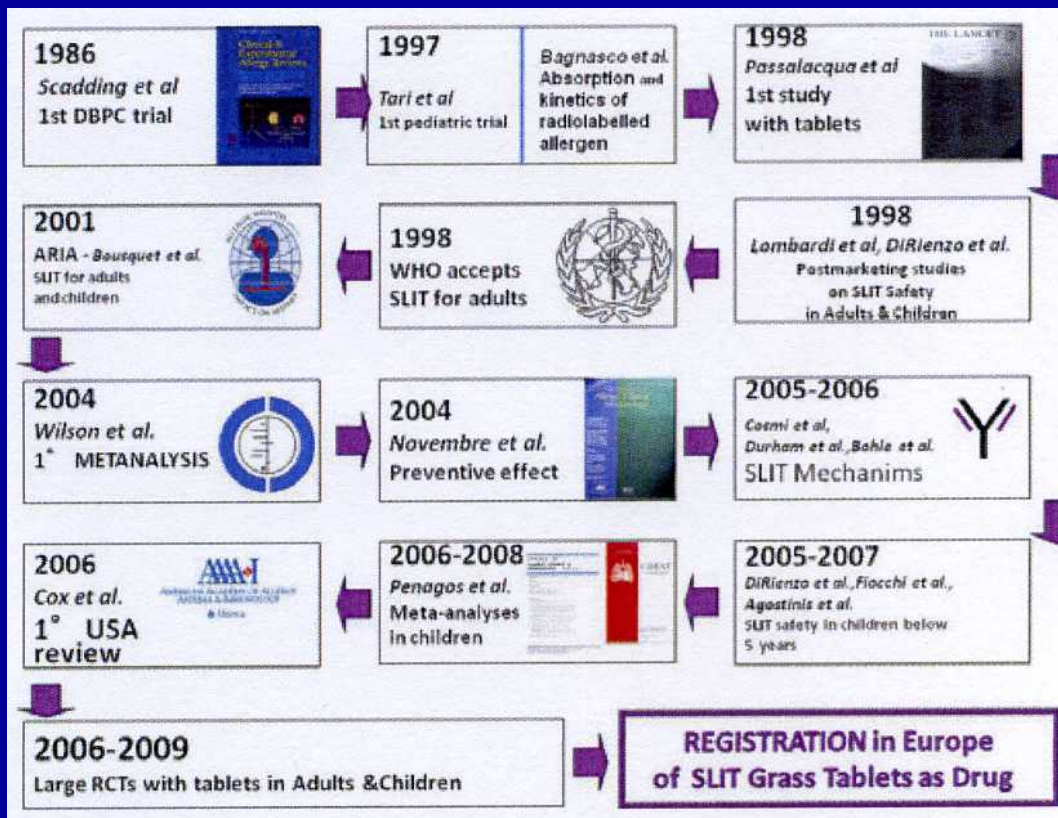
2000  
Caffarelli, Allergy  
1<sup>o</sup> study with  
tablets  
*in children*

# The contribution of carbamylated allergoid in the history of SLIT



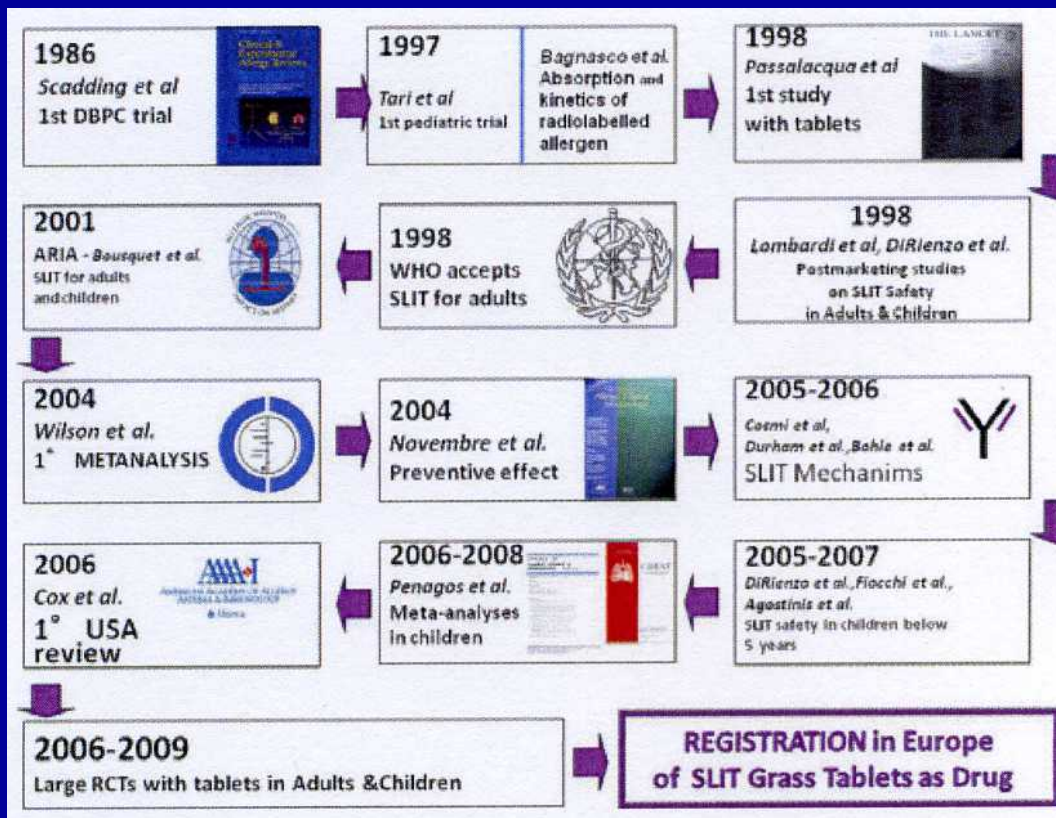
2001  
Bagnasco, Allergy  
Comparison  
between  
allergoid tablets  
VS  
allergen in tablets  
and in solution

# The contribution of carbamylated allergoid in the history of SLIT



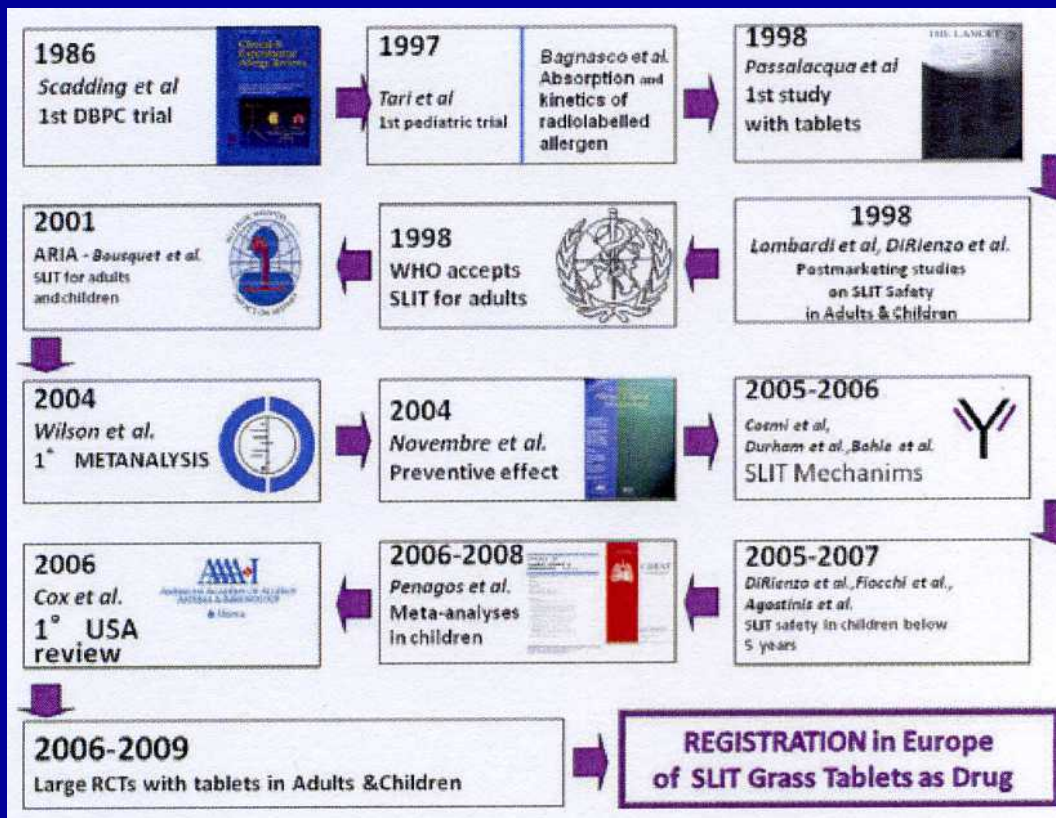
2004  
Lombardi, JACI  
Adherence  
to allergoid SLIT

# The contribution of carbamylated allergoid in the history of SLIT



2005  
Agostinis, Allergy  
Safety  
in children

# The contribution of carbamylated allergoid in the history of SLIT

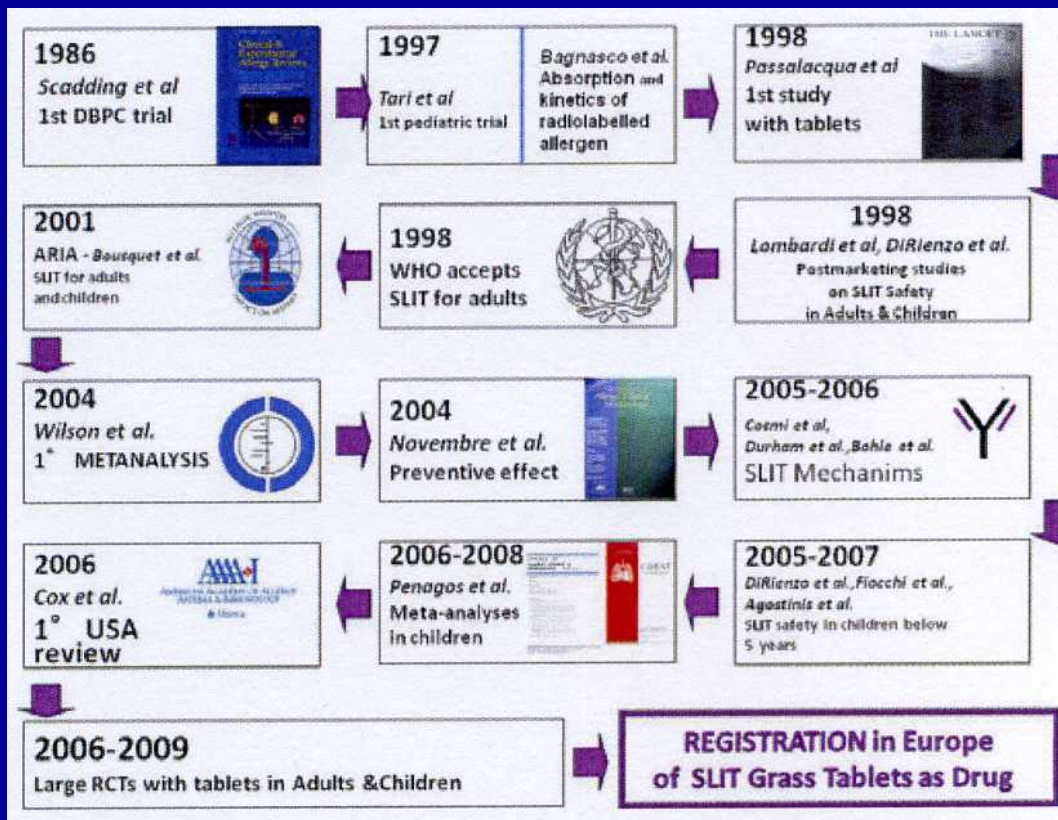


2006  
Cosmi, Clin Exp Allergy

Allergoid SLIT  
mechanism

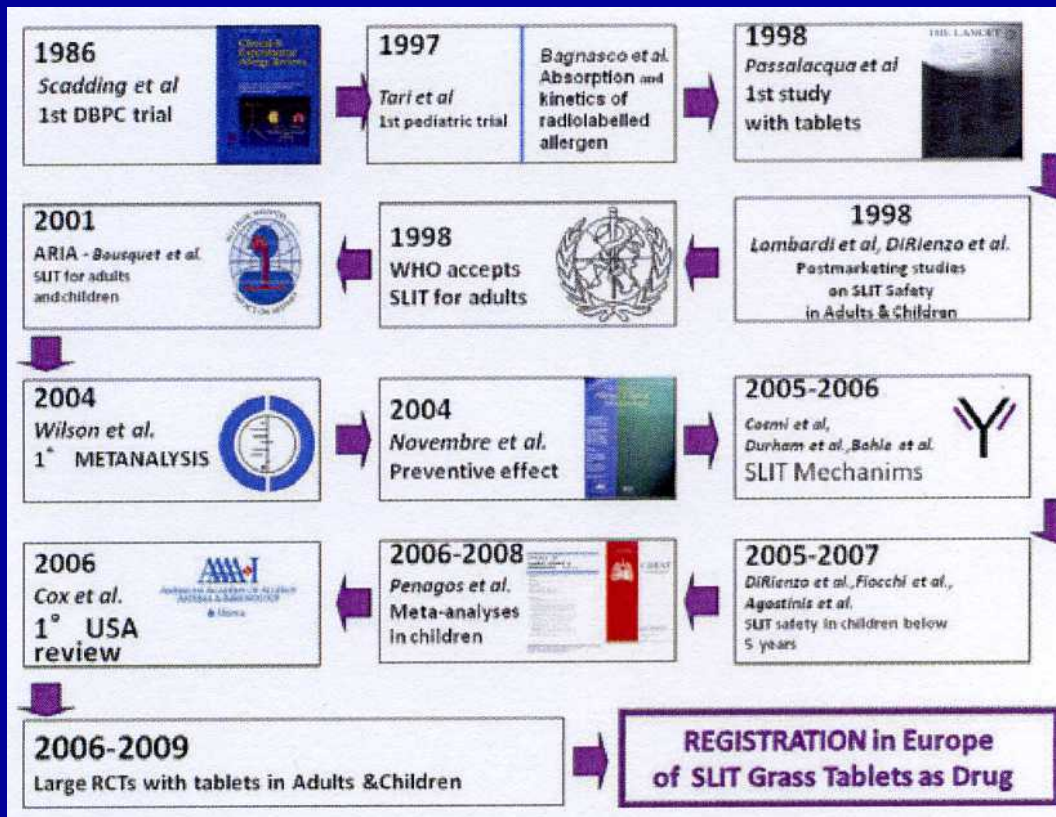


# The contribution of carbamylated allergoid in the history of SLIT



2009  
D'Anneo, Int J Imm Pharm  
Allergoid SLIT safety and tolerability with 4-day induction phase

# The contribution of carbamylated allergoid in the history of SLIT



2010  
Passali, Acta ORL

Allergoid SLIT safety and tolerability without induction phase

# A final snapshot on the market...

## Allergen SLIT

Alk - Grazax

Alk - SLITOne

Alk - SLITOne plus

Allergopharma - Allerslit

Bencard - Oralvac

HAL – Sublivac

Novartis - Tol SL

Roxall - Sulgen spray

Stallergenes - Oralair

Stallergenes - Staloral

Themocare - Allerbio sublingual

## Allergoid SLIT

Lofarma - Lais tablets

Lofarma - Lais drops