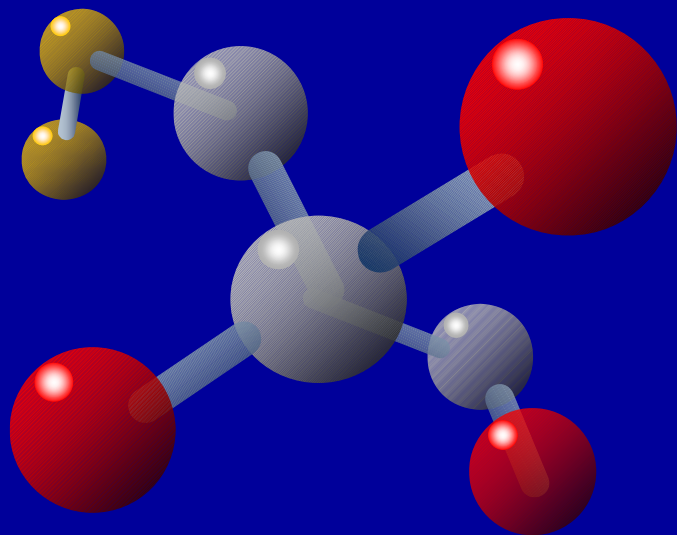


# Противоаллергические вакцины:

Активное начало важнее чем форма:  
таблетки, капли, инъекции!

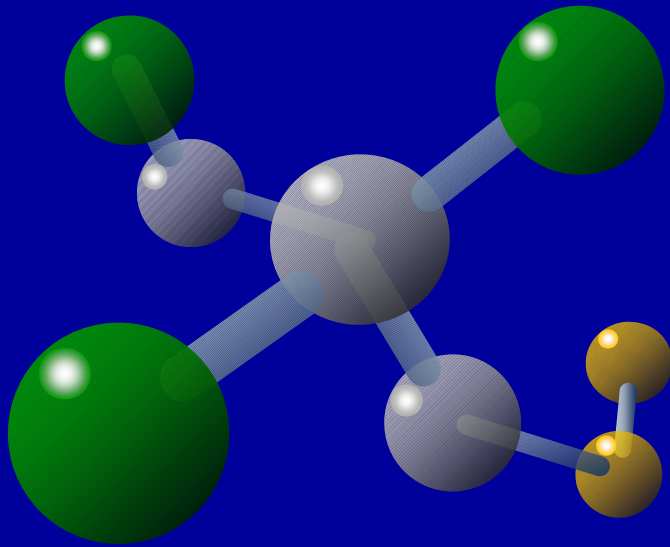
*LOFARMA S.p.A.*  
*2010*

# Аллерген



Это упрощенная  
модель молекулы  
аллергена,  
например, сорняка

# Карбамилированный Аллергоид



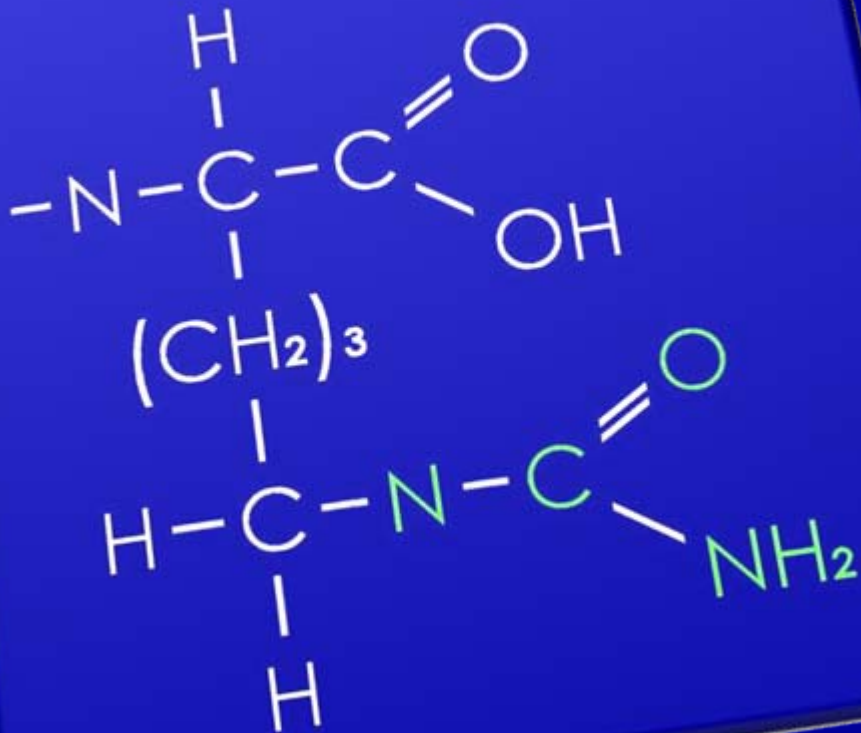
Это упрощенная модель молекулы **Аллергоида**, химически модифицированного аллергена

**Аллергоид** получают реакцией карбамилирования экстракта аллергена цианатом калия в щелочной среде, в результате чего  $\epsilon$ -аминогруппа лизина преобразуется в уреидную группу

(Mistrello et al, Allergy 1996)

# Каковы последствия ?

Carbamylated Allergoid



1

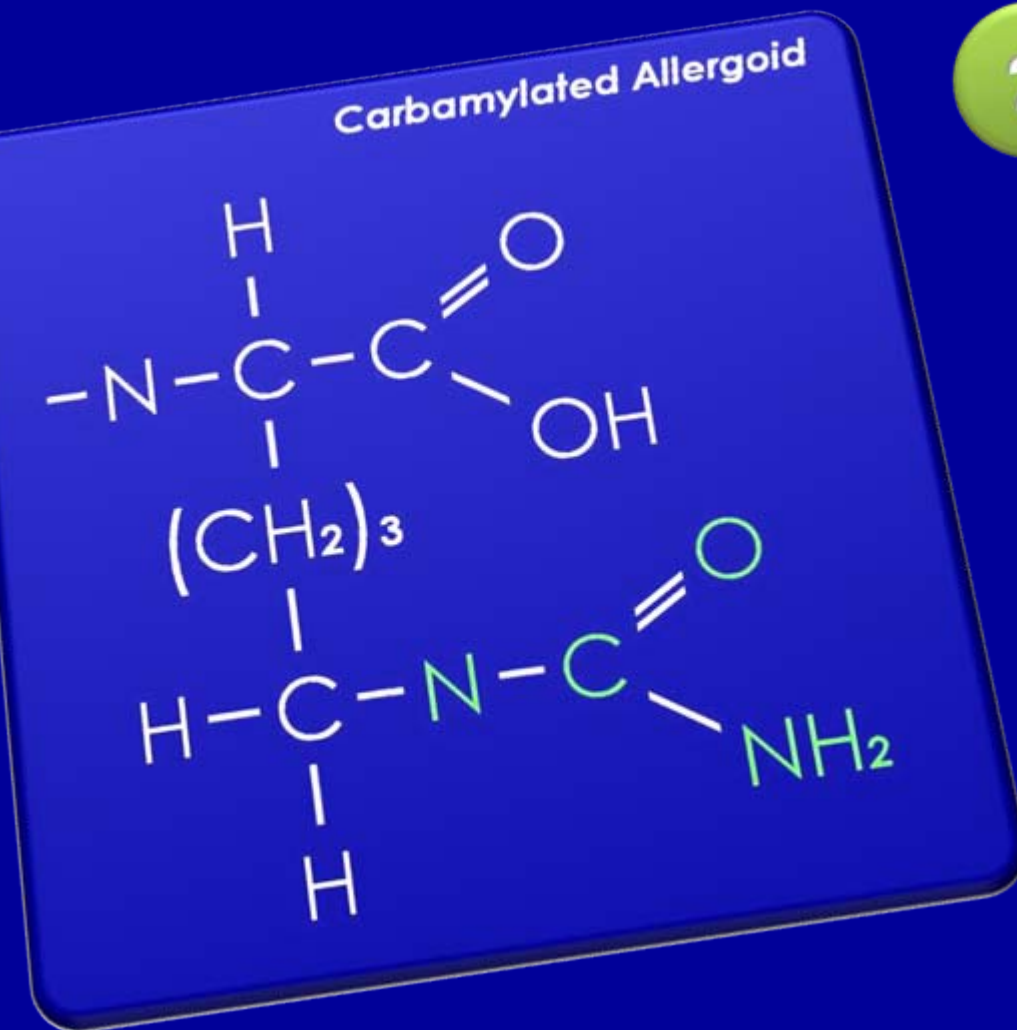
Значительное снижение  
уровня специфических IgE

Снижение аллергенной  
активности



Безопасность

# Каковы последствия ?



2

Устойчивость к ферментативному расщеплению

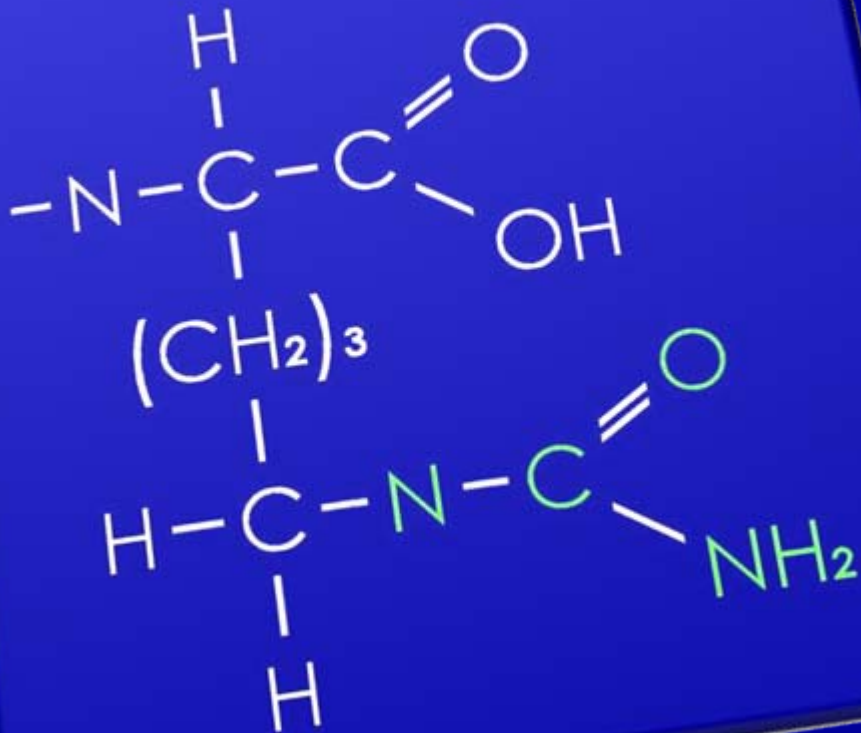
Карбамилированный аллергоид остается иммунологически активным



Нет необходимости повышать дозы  
**ЭФФЕКТИВНЫЕ ДОЗЫ**

# Каковы последствия ?

Carbamylated Allergoid



3

Изменений Т-эпитопов  
не происходит

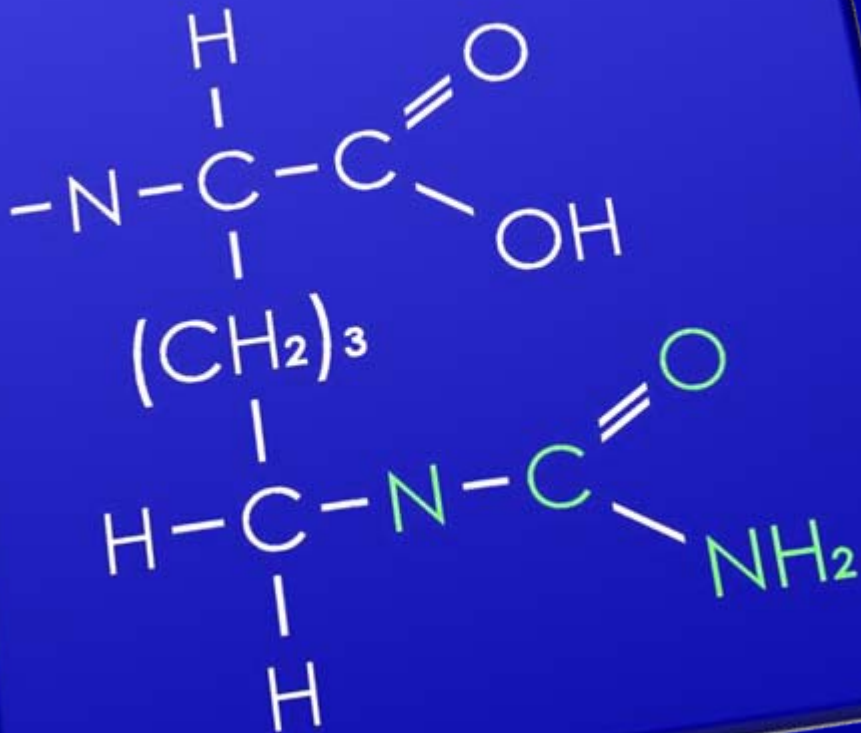
Сохранение иммуногенной  
активности



**ЭФФЕКТИВНОСТЬ**

# Каковы последствия ?

Carbamylated Allergoid



4

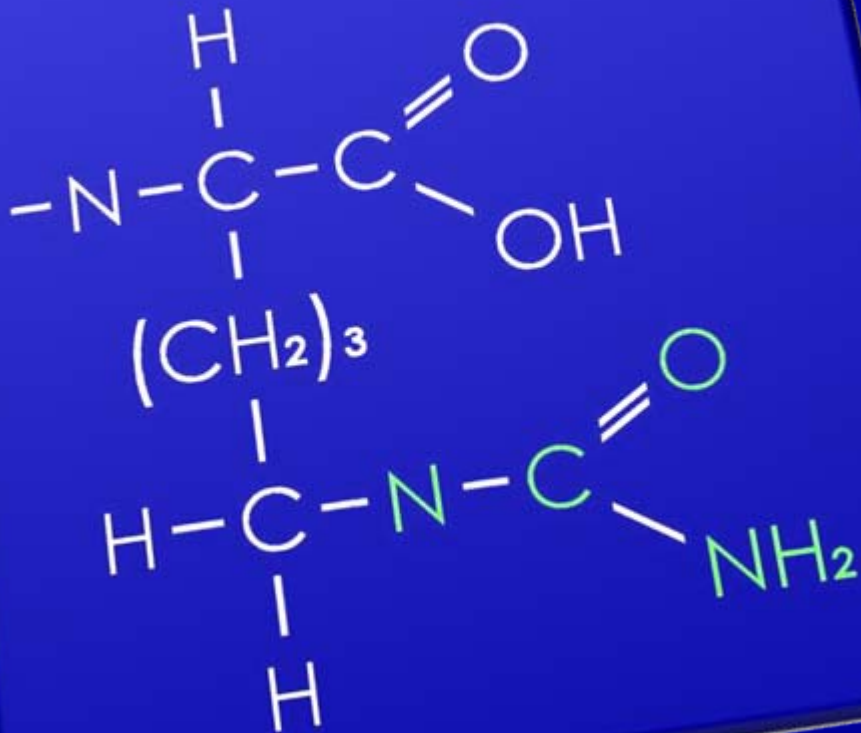
Сохранение размеров  
молекулы

Карбамилированный  
аллергоид это  
Мономерный Аллергоид

Подходит для  
СЛИТ

# Каковы последствия ?

Carbamylated Allergoid



5

Необратимость  
карбамилирования

Нет возврата к  
нативному аллергену



**БЕЗОПАСНОСТЬ**



# Список литературы:

## 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(50), Grass(75), Olive(1), birch(4), Parietaria(45) | 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(32)                          | 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+30Chiev) 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        | EAAACI 2009                                      | open                                  | adults           | 21                                     | RC and/or A          | Birch  | pre-co-seasonal           | Tab           |

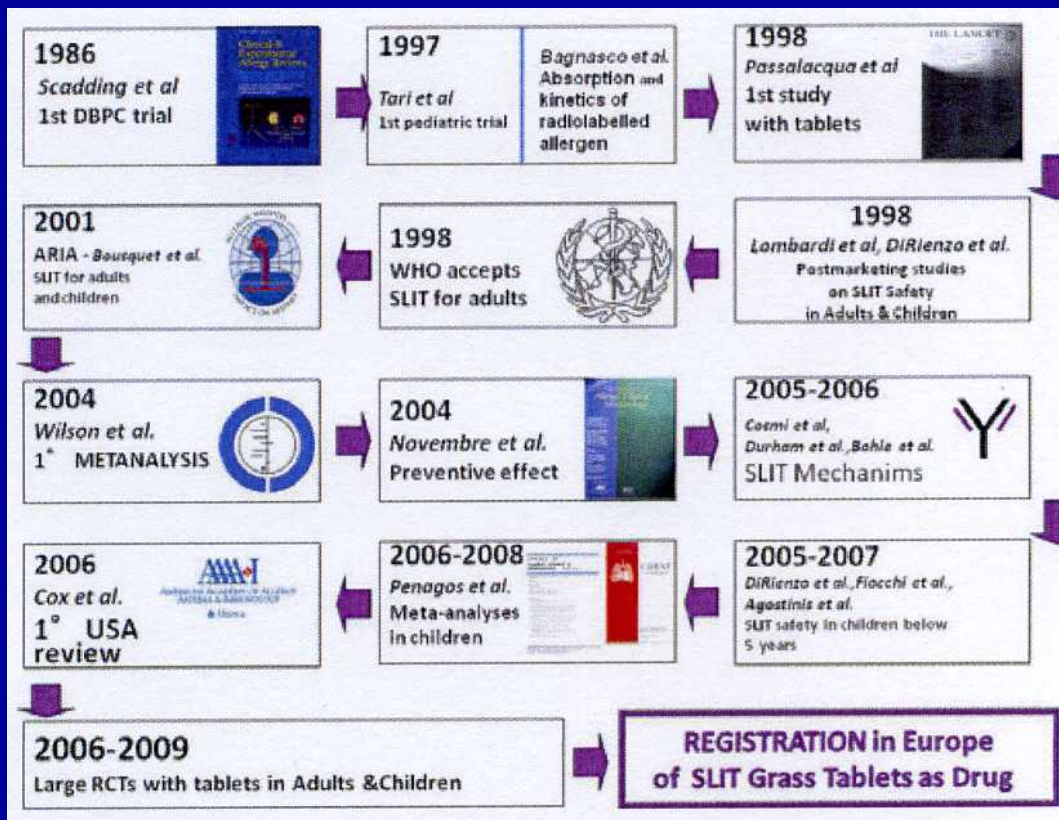
OR = Oculo-Rhinitis; A = Asthma; C = Conjunctivitis; RC = Rhino-Conjunctivitis

## 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                           |
| Cosmi        | 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        | EAAACI 2009                                      | -          | 6000/week or 2000/week  | reduction        | reduction     | -                                      | 120,000 or 208,000                |
| Fancello     | EAAACI 2008                                      | 4 days     | 1000/week               | reduction (VAS)  | -             | -                                      | 57,000                            |

# История исследований аллергоидной СЛИТ

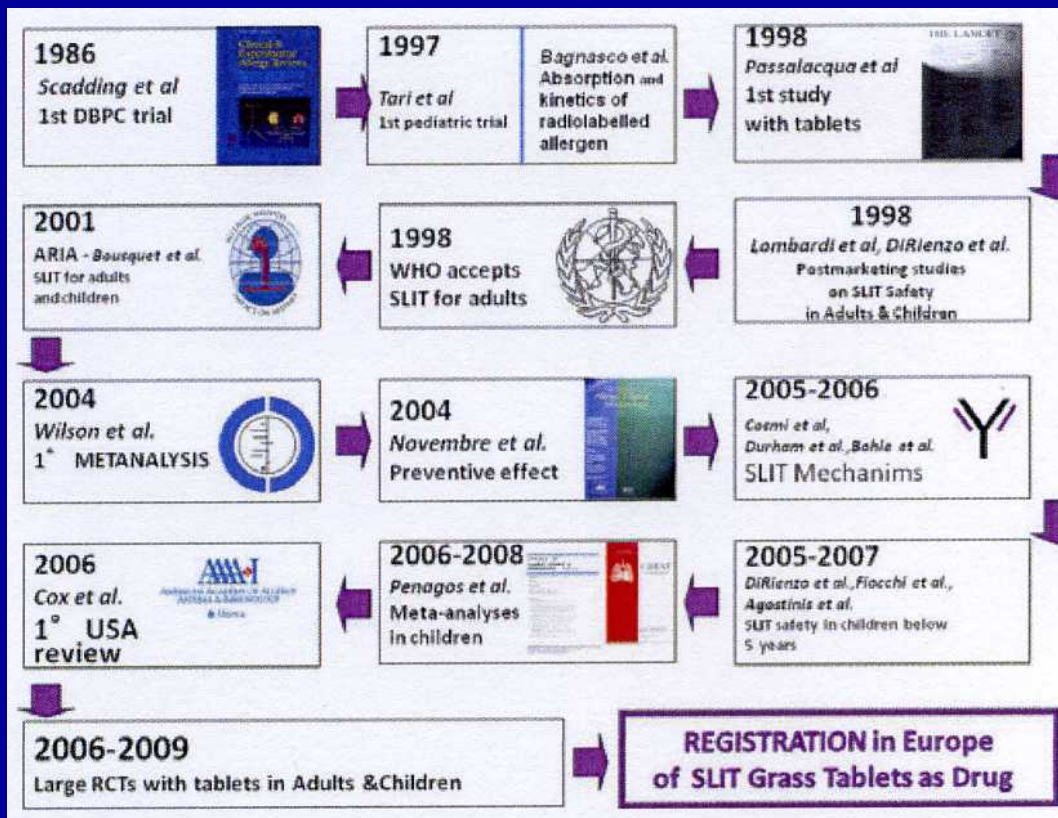


1997

Bagnasco, JACI

Изучение  
КИНЕТИКИ

# История исследований аллергоидной СЛИТ

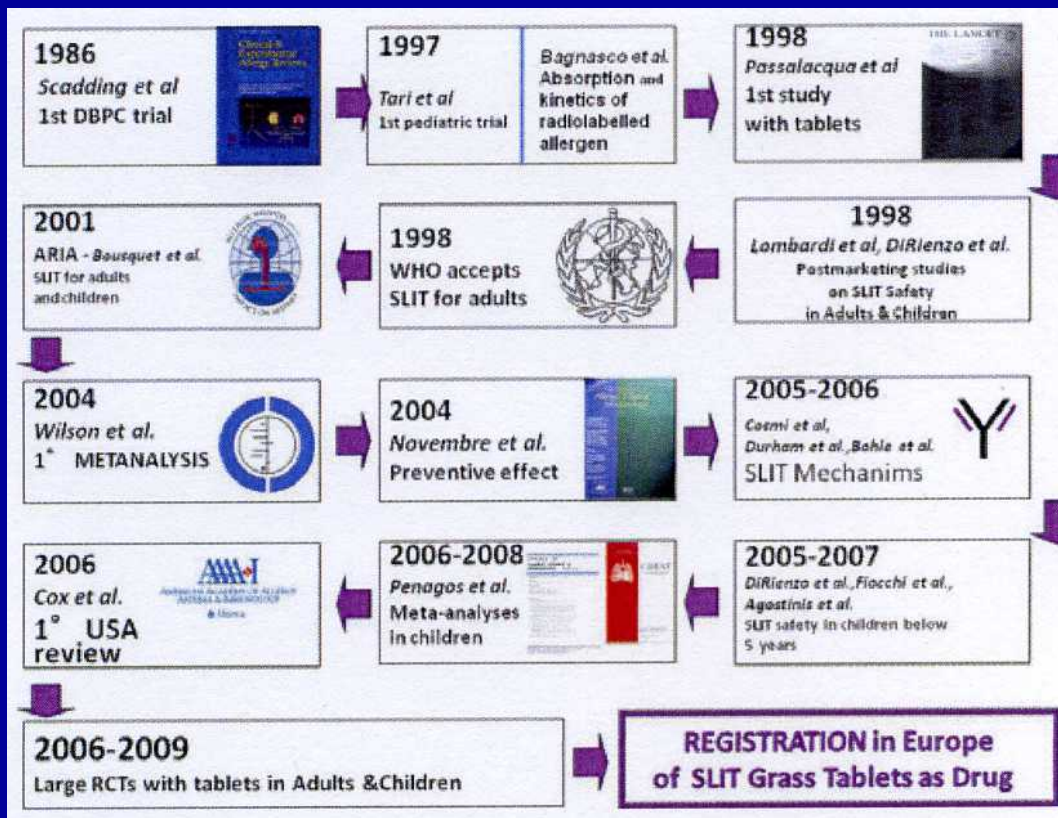


1998

Passalacqua, Lancet

Аллергоид в  
таблетках

# История исследований аллергоидной СЛИТ

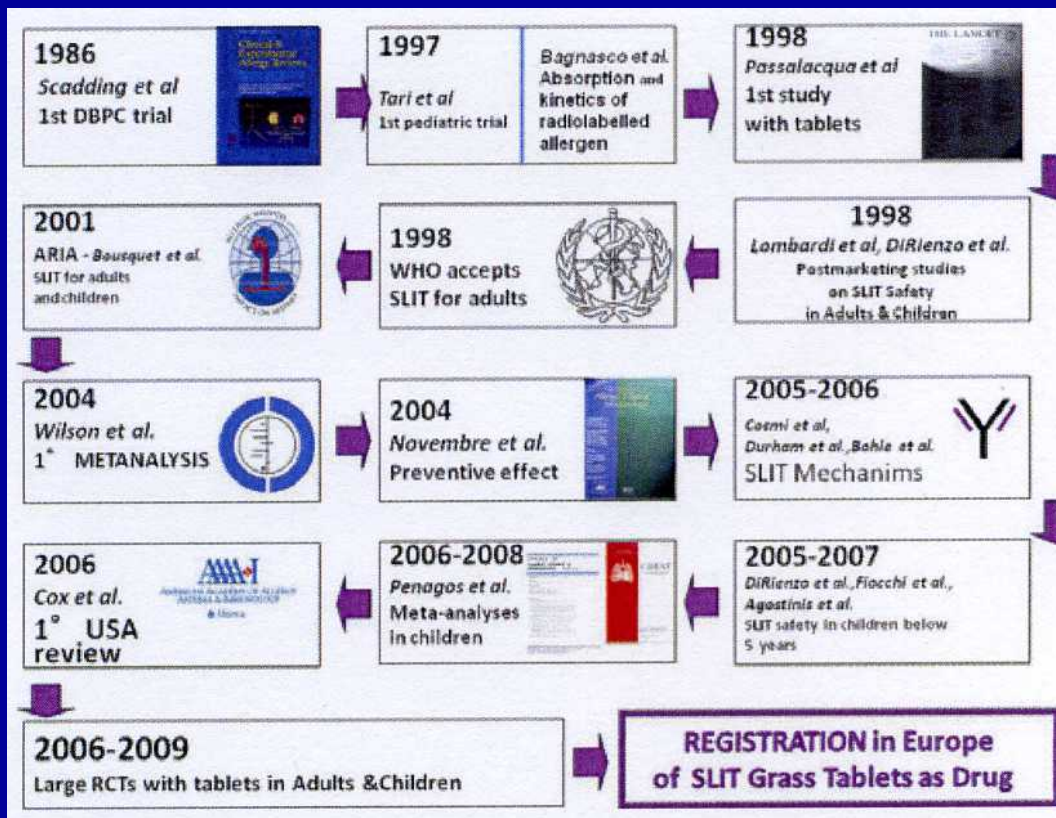


2000

Caffarelli, Allergy

Таблетки для  
детей

# История исследований аллергоидной СЛИТ

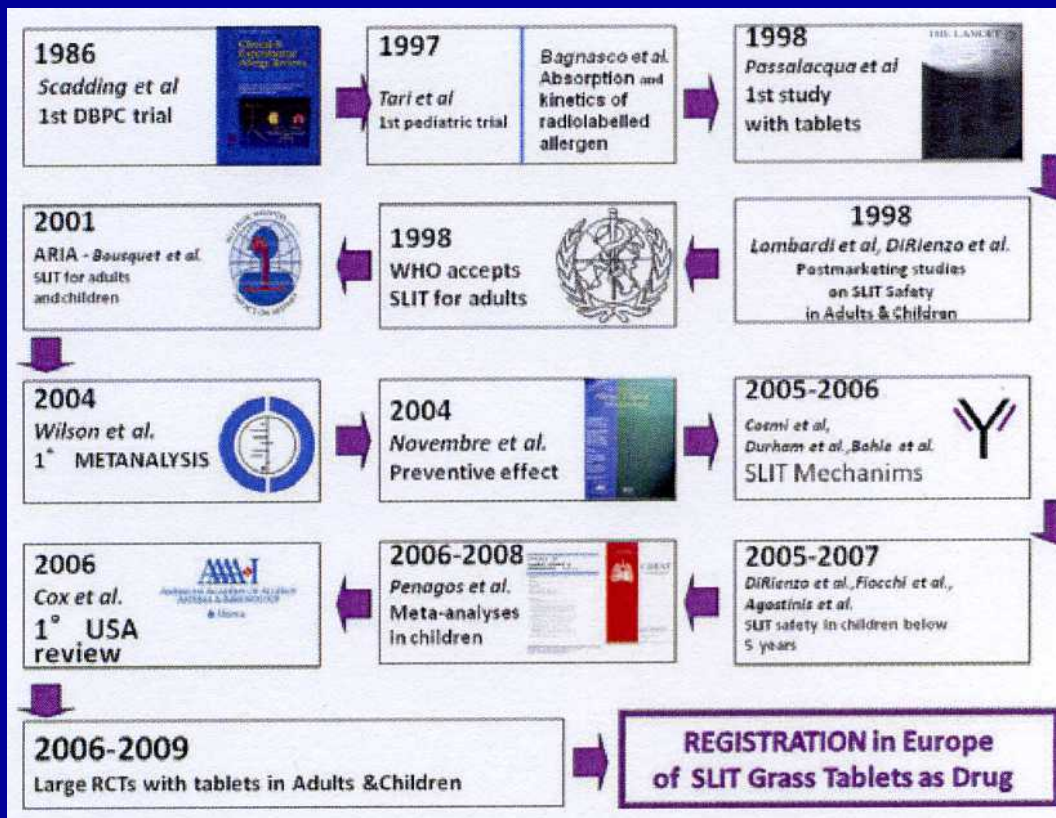


2001

Bagnasco, Allergy

Сравнение  
Аллергоида в  
таблетках с  
Аллергенами в  
таблетках и в  
растворе

# История исследований аллергоидной СЛИТ

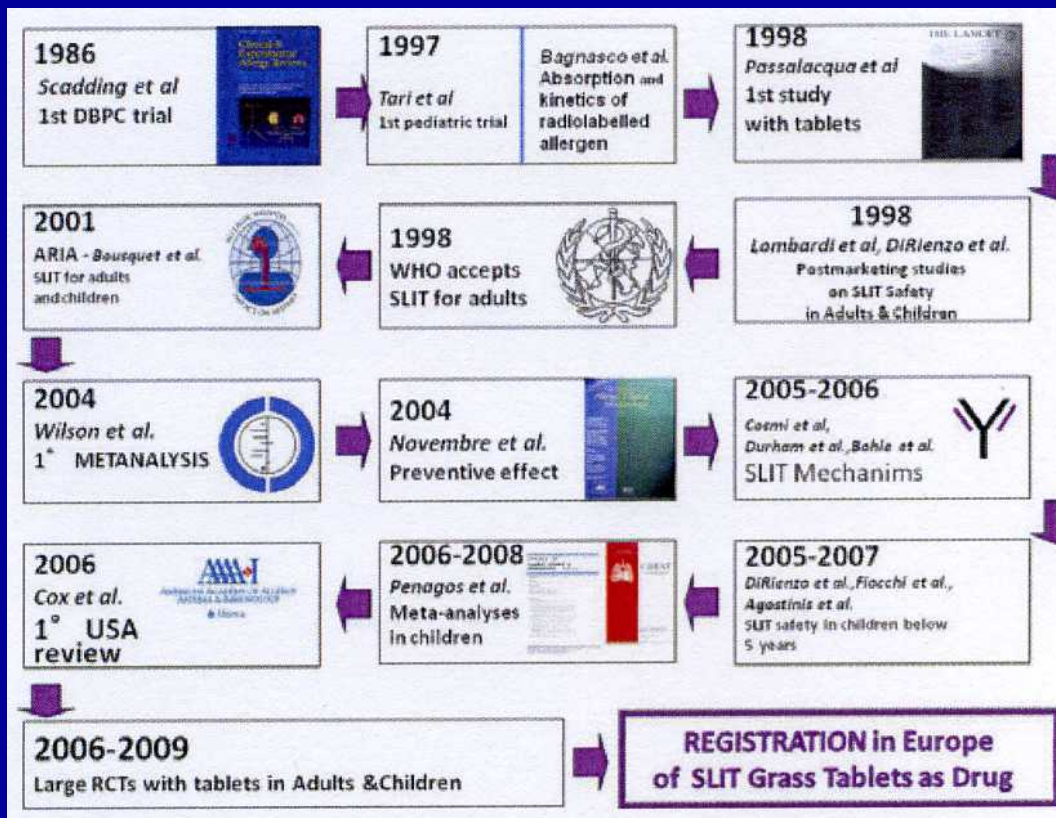


2004

Lombardi, JACI

Соблюдение  
схемы приема  
таблеток

# История исследований аллергоидной СЛИТ

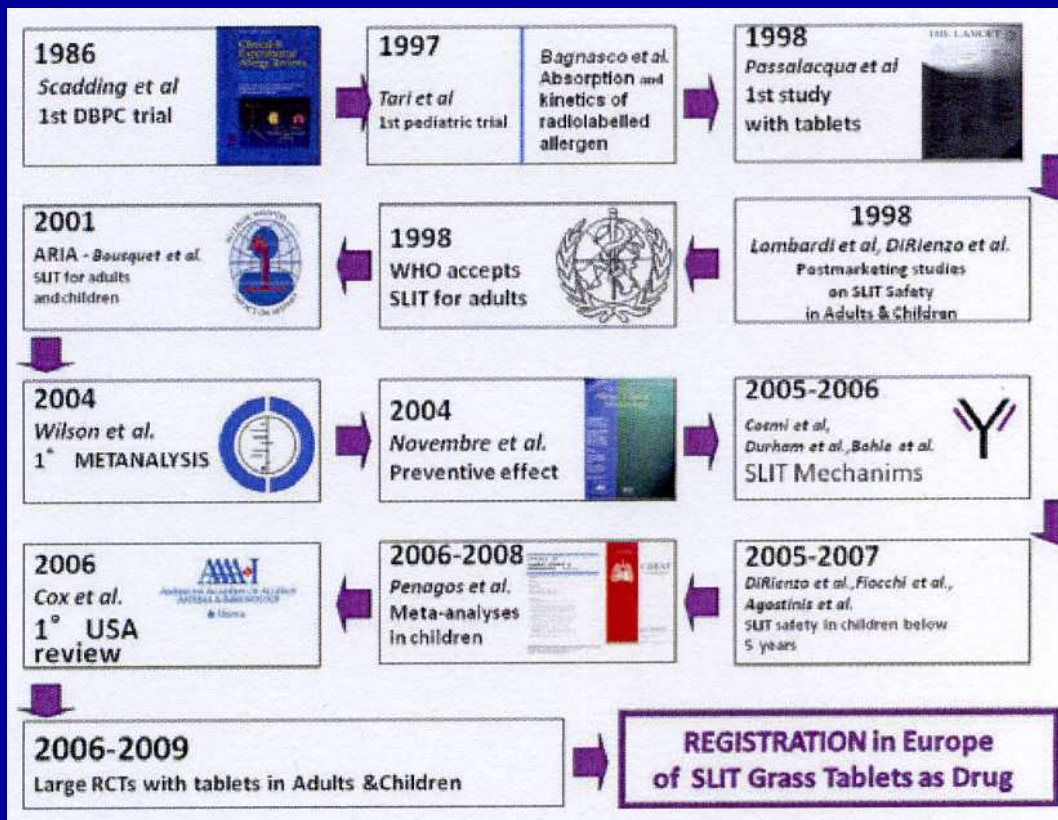


2005

Agostinis, Allergy

Безопасно для  
детей

# История исследований аллергоидной СЛИТ



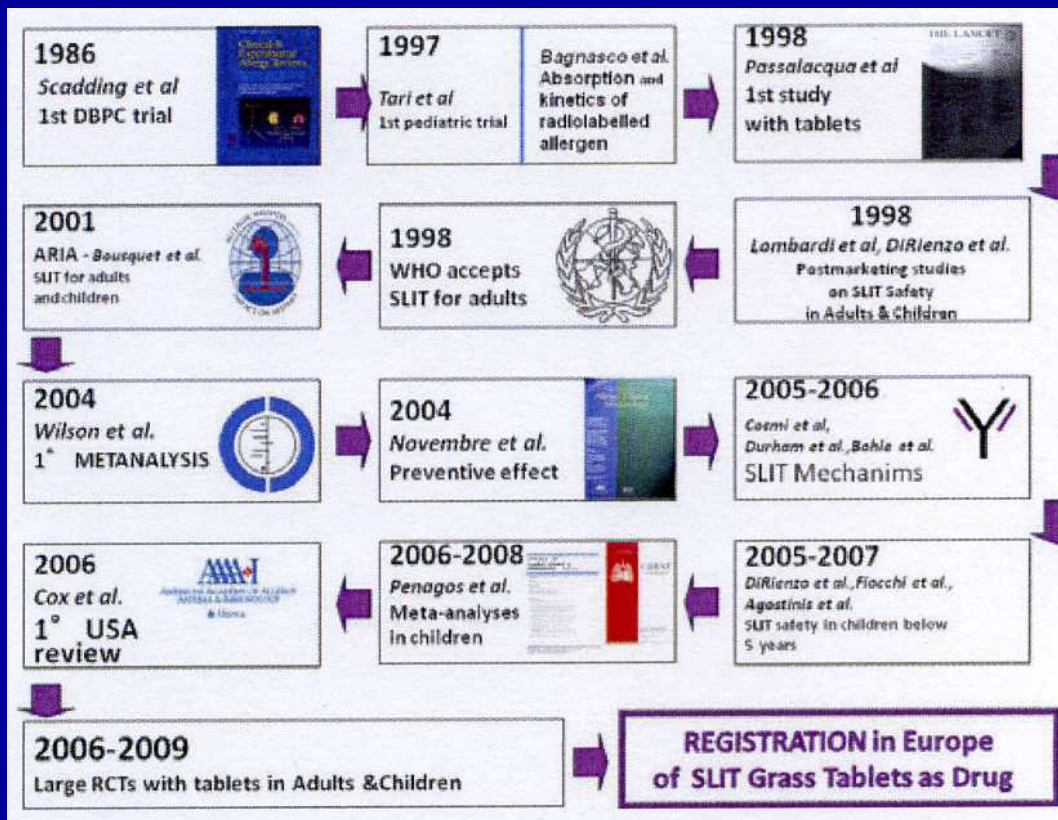
2006

Cosmi, Clin Exp Allergy

Механизм  
аллергоидной  
СЛИТ



# История исследований аллергоидной СЛИТ

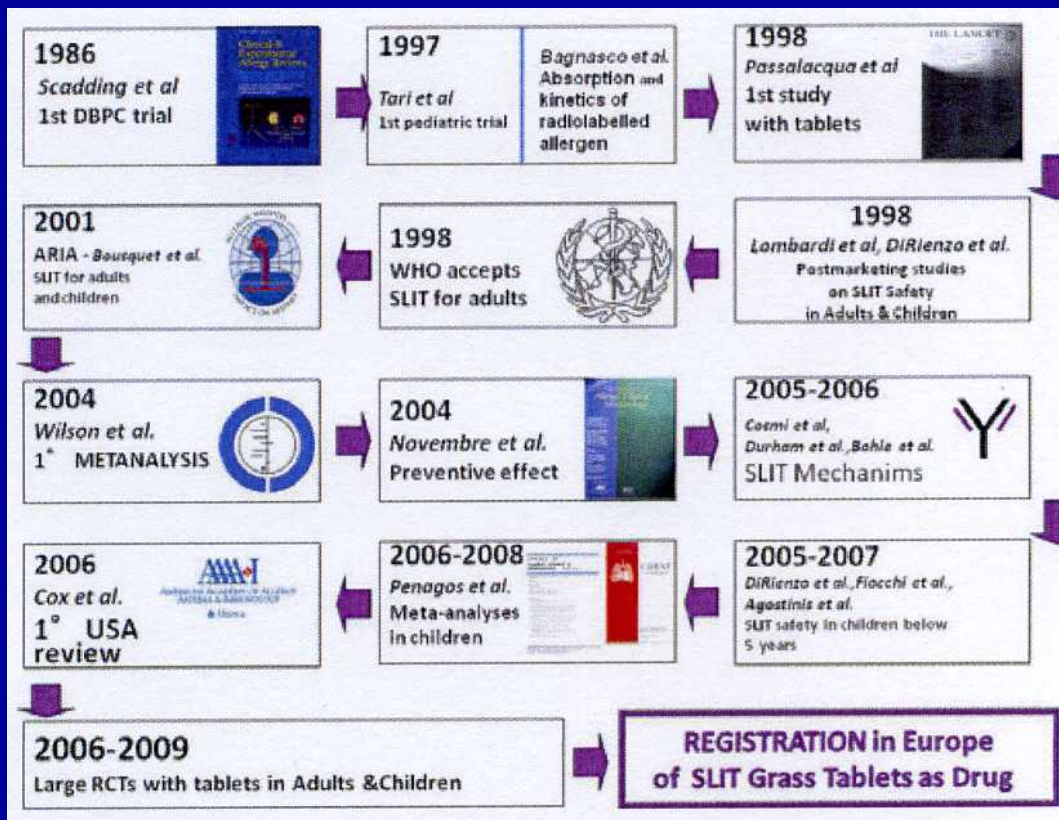


2009

D'Anneo, Int J Imm Pharm

Безопасность и  
переносимость  
аллергоидной  
СЛИТ с 4-х  
дневной  
начальной фазой

# История исследований аллергоидной СЛИТ



2010

Passali, Acta ORL

Безопасность и  
переносимость  
аллергоидной  
СЛИТ без  
начальной  
фазы

# Ситуация на рынке...

## Аллергенная СЛИТ

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

## Аллергоидная СЛИТ

Lofarma – Lais таблетки

Lofarma – Lais капли