



# play true

## CHALLENGING MEDICAL ISSUES

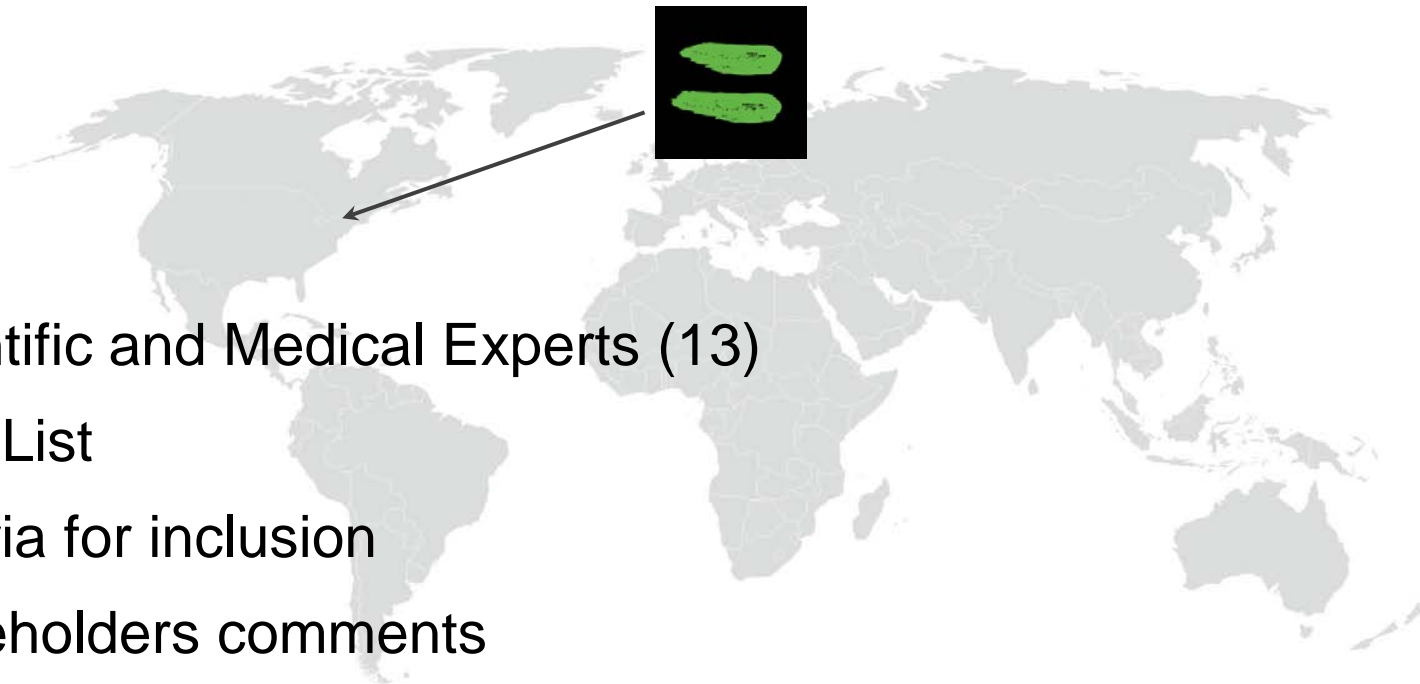
### Asthma

WADA TUE SYMPOSIUM 2014

Dr Audrey Kinahan, List Expert Group  
23 October 2014, Paris.

# The List Expert Group

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- Scientific and Medical Experts (13)
- Draft List
- Criteria for inclusion
- Stakeholders comments
- List → HMR Committee → Executive Committee → Final approval

## S3. BETA-2 AGONISTS

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All beta-2 agonists, including all optical isomers, e.g. *d*- and *l*- where relevant, are prohibited.

### Except:

- Inhaled **salbutamol** (maximum 1600 micrograms over 24 hours);
  - Inhaled **formoterol** (maximum delivered dose 54 micrograms over 24 hours); and
  - Inhaled **salmeterol** in accordance with the manufacturers' recommended therapeutic regimen.
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## S3. BETA-2 AGONISTS

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“The presence in urine of salbutamol in excess of 1000 ng/mL or formoterol in excess of 40 ng/mL is presumed not to be an intended therapeutic use of the substance and will be considered as an *Adverse Analytical Finding* unless the *Athlete* proves, through a controlled pharmacokinetic study, that the abnormal result was the consequence of the use of the therapeutic inhaled dose up to the maximum indicated above.”

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## **INHALED BETA-2- AGONISTS ON THE PROHIBITED LIST?**

**Pluim B, de Hon O, Staal B, *et al.*  
β2-Agonists and Physical  
Performance: A Systematic Review  
and Meta-Analysis of Randomized  
Controlled Trials. *Sports Med.* 2011**



# Salbutamol

## THRESHOLD APPROACH



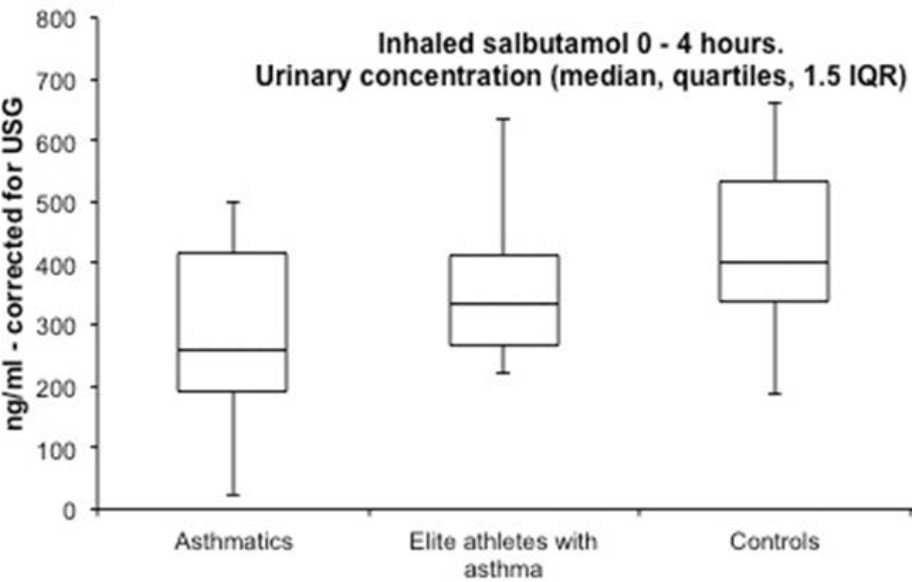
### Permitted

Inhaled doses  $\leq 1600$  mcg/ 24 hours  
< 1000 ng/mL in urine

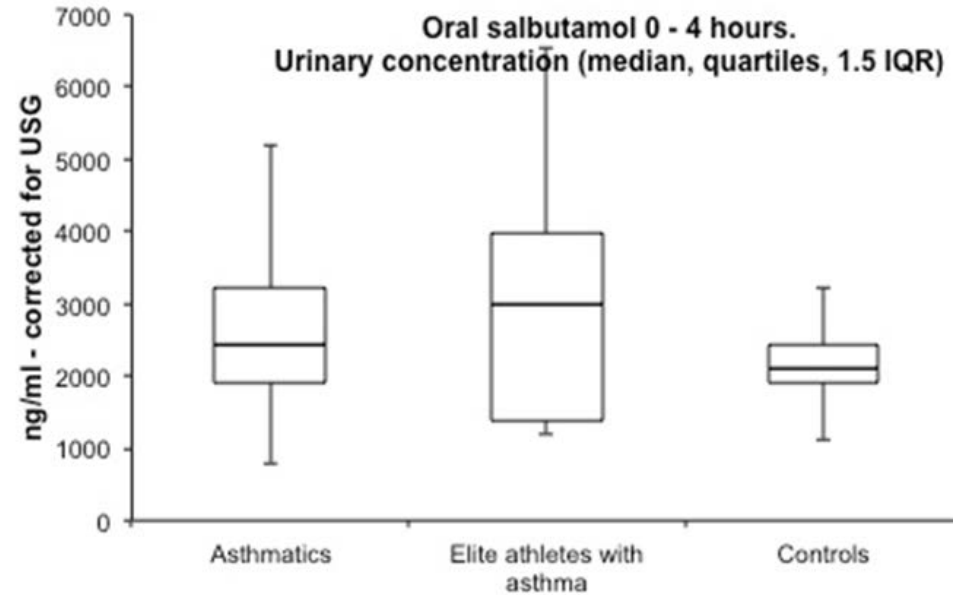
### Prohibited

Oral, IV,  
Inhaled doses >1600 mcg/ 24 hours  
>1000 ng/mL in urine  $\rightarrow$  PK study

# Urinary concentrations: Inhaled & Oral Salbutamol



Inhaled salbutamol 0.8 mg



Oral salbutamol 8 mg

# Formoterol

## CORRELATION BETWEEN INHALED DOSE AND URINE CONCENTRATION



### Permitted

Inhaled delivered dose  
 $\leq 54$  mcg/ 24 hours  
< 40 ng/mL in urine

### Prohibited

Inhaled delivered dose  
> 54 mcg/ 24 hours  
> 40 ng/mL in urine

→ PK study

2012 List: Threshold 36 mcg/24 hours,  
correlated with urinary threshold of 30 ng/ml



# Salmeterol

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**Permitted** Usual inhaled dose of 50 mcg *bd*\*,  
Severe cases –

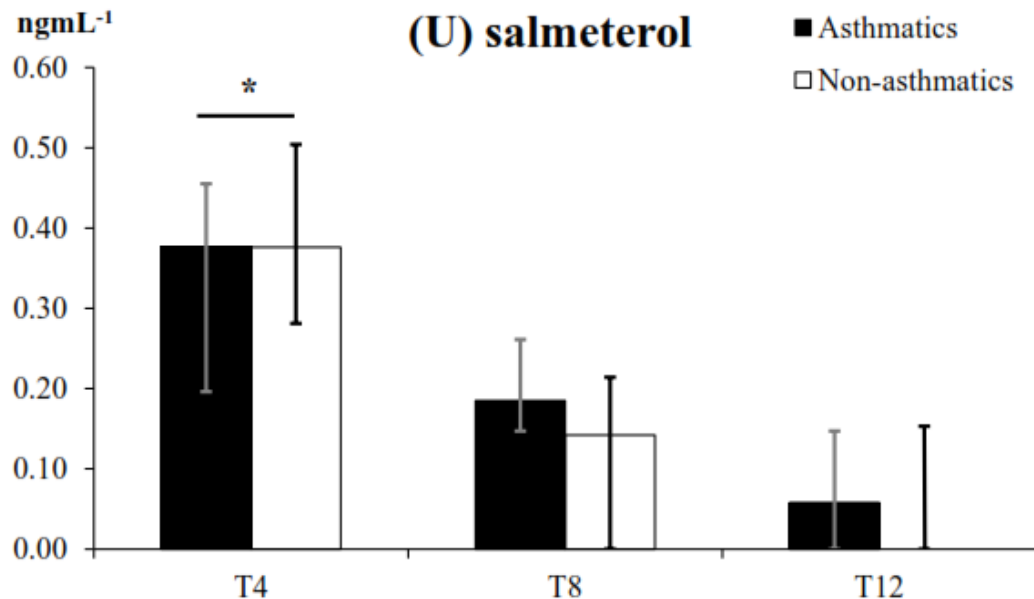
Max dose 100 mcg *bd*\*

**Prohibited** Doses in excess of 100 mcg *bd*

\*Manufacturer's recommended therapeutic dose may change from country to country



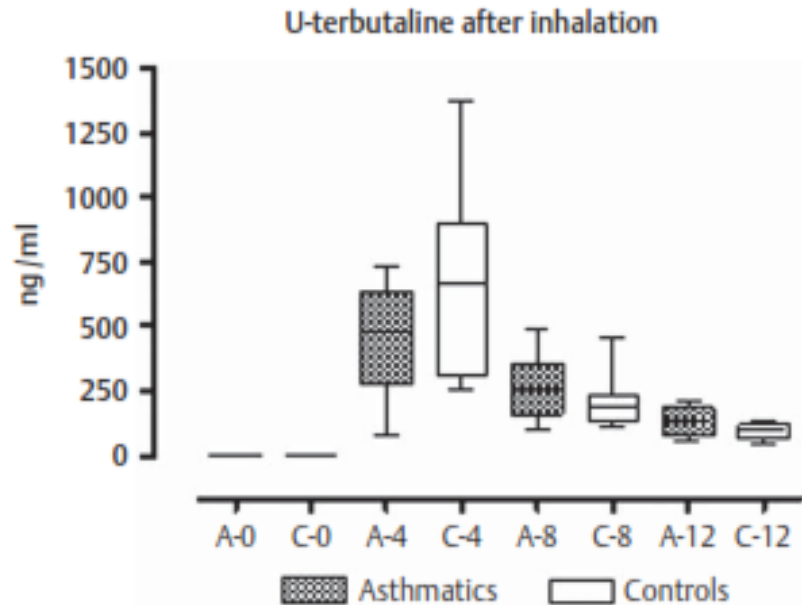
# Urinary concentrations: Inhaled Salmeterol 100 mcg



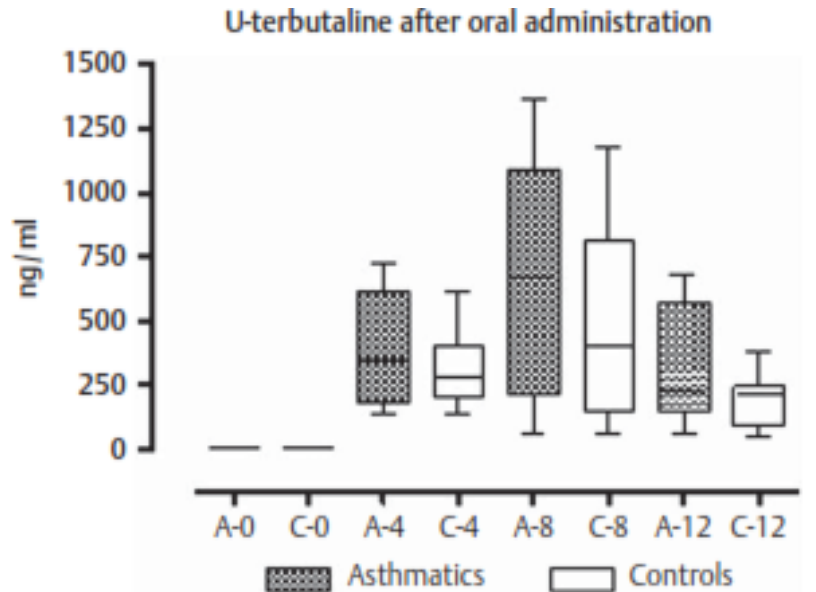
Highest observed individual urine concentration of salmeterol was 0.74 ng/mL when not corrected for USG

Urine Concentrations of Inhaled Salmeterol and its Metabolite  $\alpha$ -Hydroxysalmeterol in Asthmatic and Non-Asthmatic Subjects Hostrup *et al.*, J Sports Med Doping Stud 2:110, doi:10.4172/2161-0673.1000110

# Urinary concentrations: Inhaled & Oral Terbutaline



Inhaled Terbutaline 2 mg

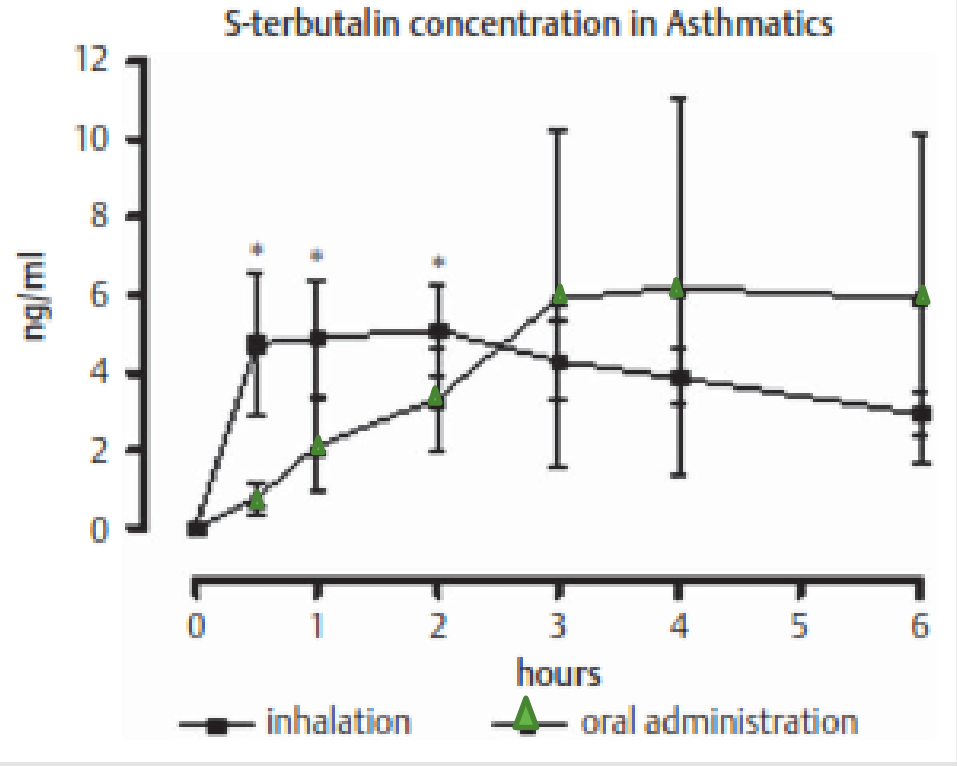


Oral Terbutaline 10 mg

# Serum concentrations: Inhaled & Oral Terbutaline

Inhaled repeat doses  
Terbutaline 1 mg every  
2 hours, total 4 mg

Oral Terbutaline 10 mg



Urine and Serum Concentrations of Inhaled and Oral Terbutaline, J. Elers *et al*, Int J Sports Med 2012; 33(12): 1026-1033 doi: 10.1055/s-0032-1311590

# All other Beta-2-agonists

## PROHIBITED

- Fenoterol
- Reproterol
- Procaterol

## Ultra-Long Acting Beta- 2-Agonists

- Indacaterol (Onbrez® & Ultibro®)
- Vilanterol (Relvar® & Anoro®)
- Olodaterol (Striverdi®)

