



We will begin momentarily at 2pm ET



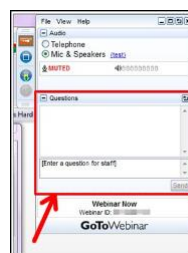
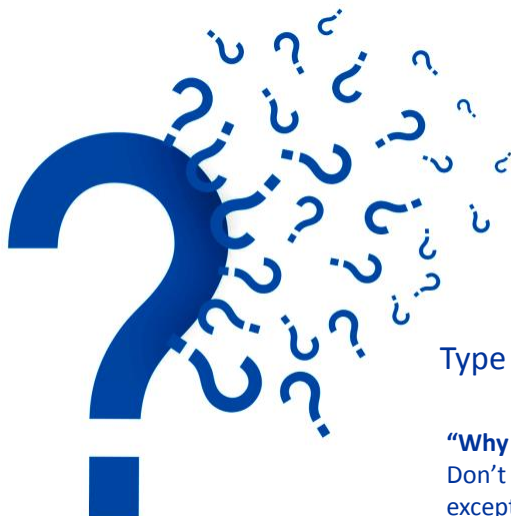
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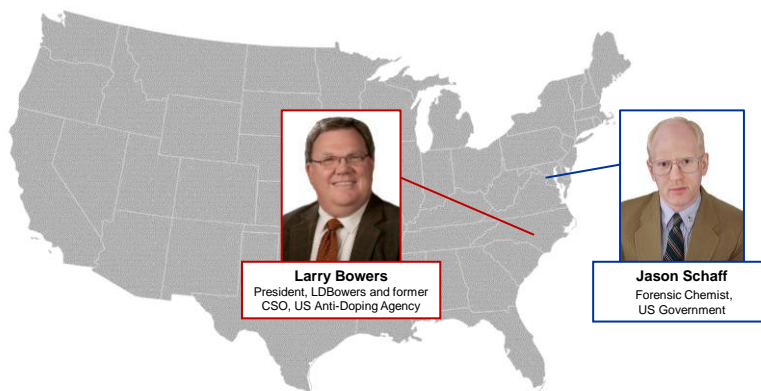


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“Chemistry of Anti-Doping: Deterring of Performance-Enhancing Drug Use by Athletes”

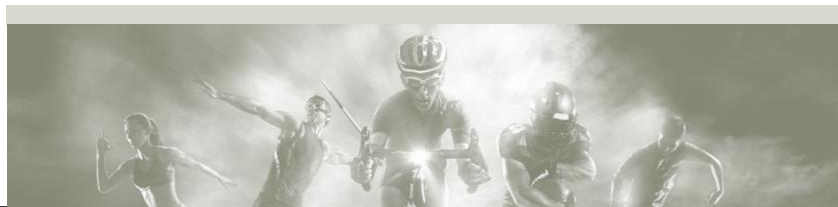


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Chemistry of Anti-Doping:

Detering Performance-Enhancing Drug Use by Athletes

Larry D. Bowers, PhD



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Why do athletes dope?

- ▣ It works!
- ▣ **There are powerful incentives to dope**
 - ▣ Lack of trust that others will not dope and thereby defraud the individual of their legitimate rewards
 - ▣ Concern that anti-doping programs do not catch cheaters
 - ▣ Concern that the sport organization is not committed to eliminating doping
 - ▣ Concern that some countries are not committed to eliminating doping
 - ▣ Huge personal and financial rewards
 - ▣ Immediate gratification versus delayed sanction (time discounting)
 - ▣ "Win at all costs" mentality



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Doping is a rational choice

- Decision regarding doping behavior is made by evaluating the rewards versus risks
- **Doping is**
 - Instrumental
 - Communal
 - Requires expertise



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Compliance and Sanction Threats

- Deterrence is based on threat assessment
 - **Certainty of being detected and sanctioned**
 - Severity of sanction
 - Timeliness (Celerity) of sanction
- Perceptions are more important in decision making than facts
 - Perceptual calibration
 - Perceptual deterrence
 - Perceptual (experiential) re-calibration





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Is Random Drug Testing a Threat?

Assume that an individual uses a drug **three times a month**. The detection window for the drug is **two days**.

Assume that the drug testing program tests **5%** of the eligible pool of athletes at random each month.

How long does it take to detect this drug user?

JULY 2017						
SUN	MON	TUE	WED	THU	FRI	SAT
						1
2		3	Test?	Test?	5	6
7	8	9	10	11	12	13
14	15	16	17	18	19	20
21	22	23		24	Test?	Test?
27	28	29	30	31		



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Audience Challenge Question

ANSWER THE QUESTION ON BLUE SCREEN IN ONE MOMENT

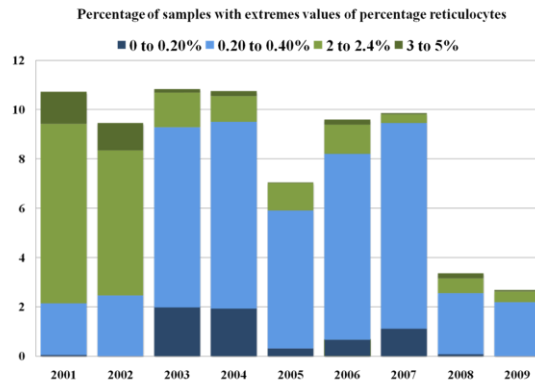


How long does it take to detect this drug user?

- 4 months
- 9 months
- 4 years, 9 months
- 9 years, 4 months
- 19 years, 4 months

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Does testing change behavior?



Zorzoli M, Rossi F. *Drug Test Anal* 2010; **2**: 542-7.

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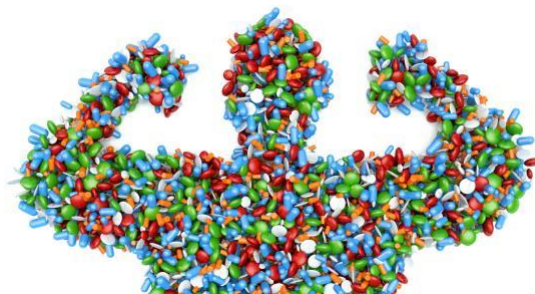
How can we influence perceptions?

- **Perceptual re-calibration – ensure that experience with the system reinforces the certainty of being caught**
 - **Research** to improve detection of doping agents
 - **Research** to identify new doping agents
 - Collection of information to guide testing strategies
 - “Non-analytical” cases

- **Ambiguity aversion – uncertain situations increase certainty of detection**
 - No-advance-notice out-of-competition sample collection
 - Alternative matrices (e.g., dried plasma spots) to cost-effectively increase testing numbers



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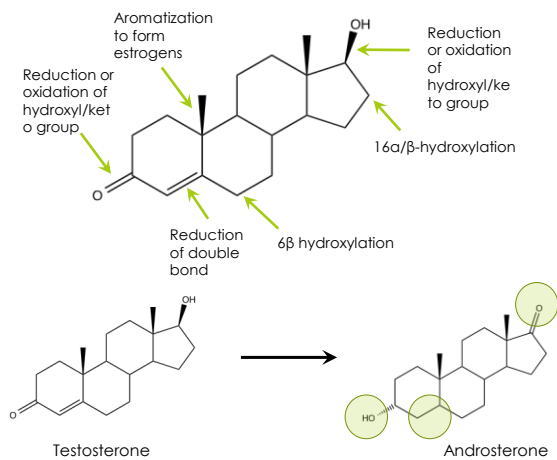


Synthetic anabolic steroid detection



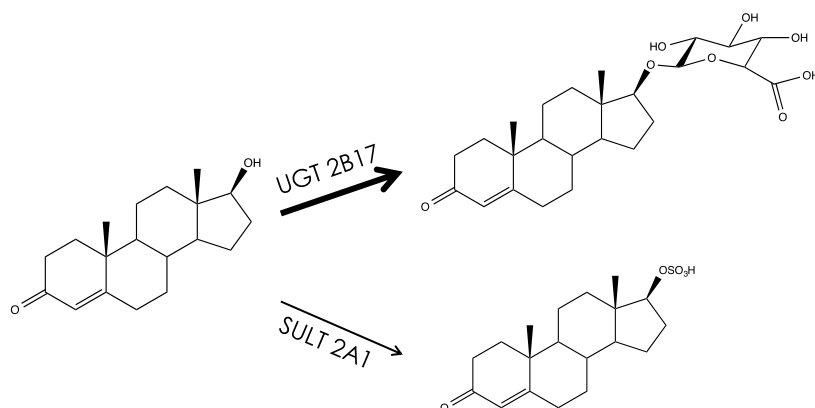
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Steroid Metabolism (Phase I)



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Steroid Metabolism (Phase II)



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Audience Challenge Question

ANSWER THE QUESTION ON BLUE SCREEN IN ONE MOMENT



Synthetic anabolic steroids can be detected in urine for how long after administration?

- Several days
- Several weeks
- Several months
- Several years

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Detection of Urinary Steroids

GC - MS and GC - MS/MS

- SPE sample clean-up
- @glucuronidase cleavage
- Extract free steroids with *t*-butyl-methyl ether or pentane
- Derivatization with MSTFA/ $\text{NH}_4\text{I}/\text{C}_2\text{H}_5\text{SH}$
- GC - MS SIM analysis

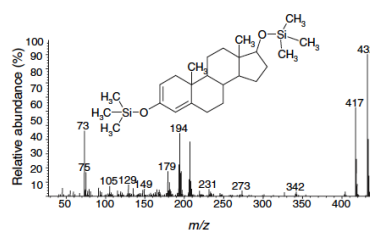
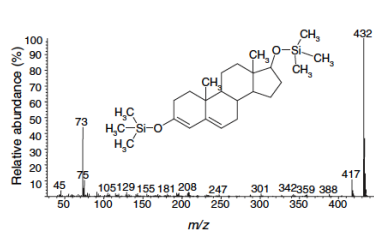
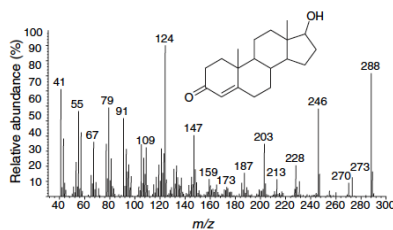
HPLC - MS/MS

- SPE sample clean-up
- Optional conjugate cleavage
- Extract free steroids
- LC - MS/MS analysis

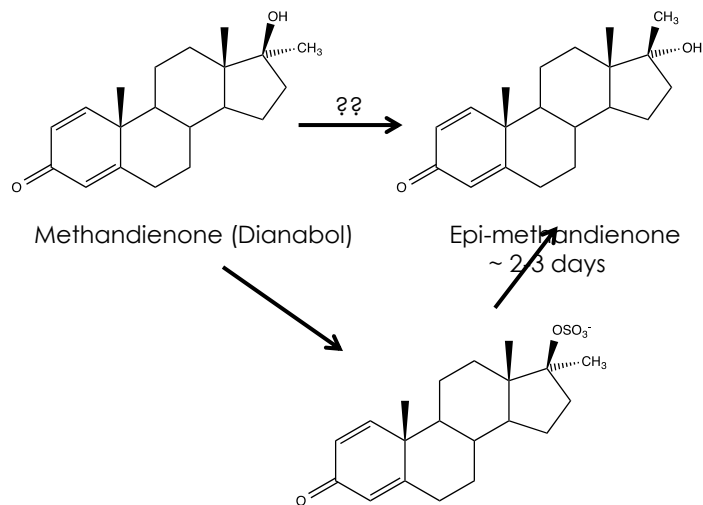


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Pros & Cons of Derivatization



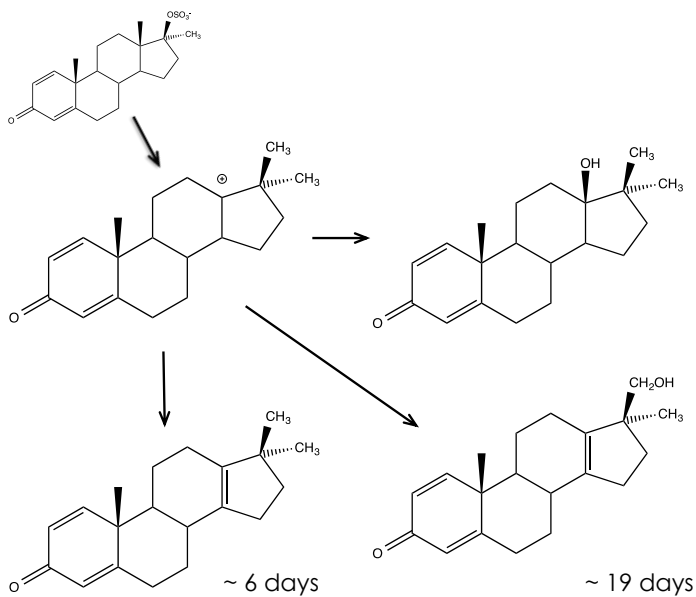
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Edlund PO, Bowers LD, Henion, JD. *J Chromatogr* 1989; **487**: 341-56.



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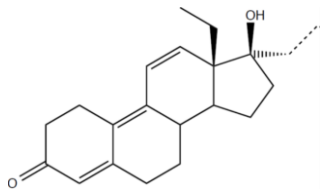


Schänzer W et al. *Rapid Commun Mass Spectrom* 2006; **20**: 2252-8.

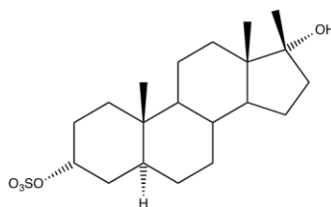


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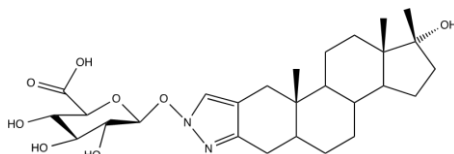
Long-lived Steroid Metabolites



Tetrahydrogestrinone (THG)



Tetrahydro-epi-methyltestosterone-3-sulfate

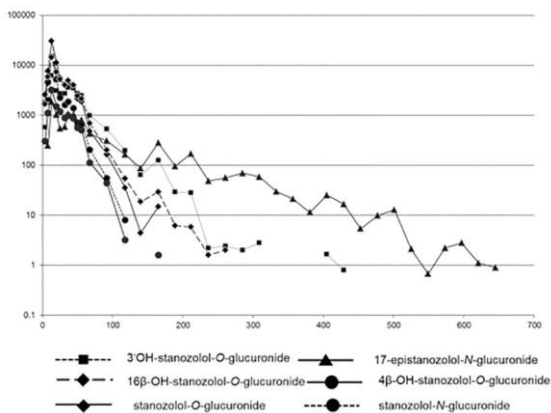


17-epi-stanozolol-N-glucuronide



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Detection Window for Stanozolol Glucuronide Conjugates



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Challenges with long-lived metabolite analysis

- Decreasing limits of detection and identification of long-lived metabolites allows detection of anabolic steroids for many months
- Re-analysis of samples from past Olympic Games results in more positive urine samples and medal re-distribution
- Detection of pg/mL metabolites in urine raises interpretive challenges
 - Residual metabolites versus new use
 - Inadvertent ingestion of contaminated meat or grain
 - "Off-label" medical treatment (e.g., clomiphene for male infertility)



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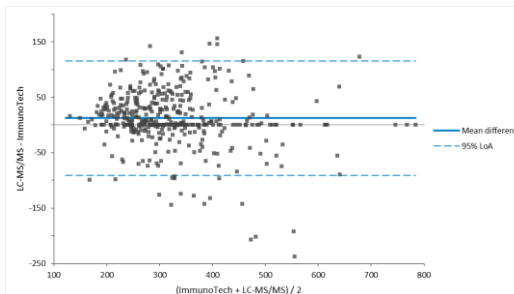
Peptide and protein doping agent detection



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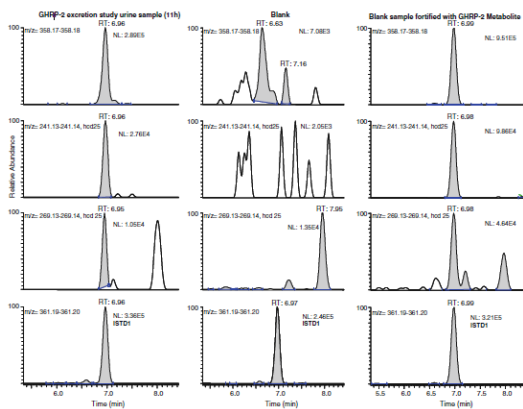
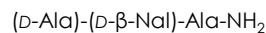
LC-MS/MS Quantification of IGF-1

- Interlaboratory (n=5) study of IGF-1 bottom-up method
- Working group has developed serum reference material with a consensus concentration assigned for LC-MS/MS work
- Collaborating with the National Institute for Science and Technology (NIST) to develop an ISO traceable serum-based reference material



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Urinary Analysis of GHRP2



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Summary and Conclusions

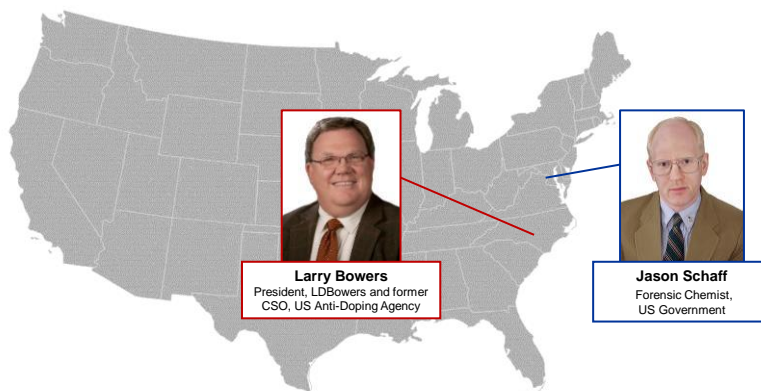
- Doping/cheating in sport is a reflection of society and its problems as a whole
- Anti-doping policies should be designed to deter the use of performance-enhancing drugs and involve complex interdisciplinary effort
- Perceptual deterrence model provides guidance for optimizing programs to achieve behavior change
- Research is an important factor in increasing the perceived certainty of detection, which is the primary factor in assessing risk
- Anti-doping testing requires a skilled laboratory staff with expertise in analytical science, biochemistry, clinical chemistry, exercise physiology, pharmacology, hematology, and endocrinology



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- Average award: \$202,000 USD
- Funding decisions made in 4-5 months
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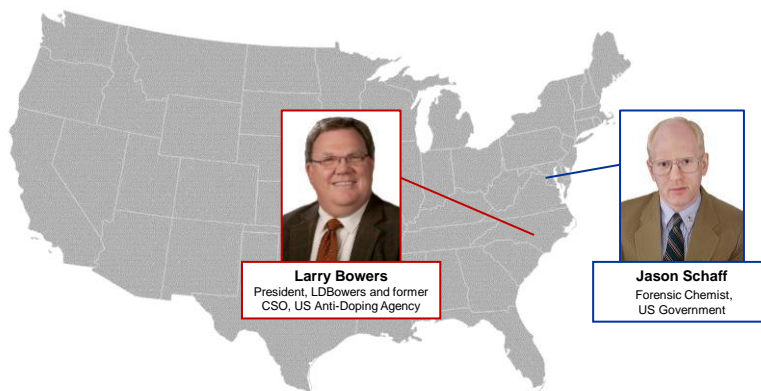
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