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RECENT ADVANCES IN DOPING ANALYSIS (9)

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Sydney Olympics 2000: An Overview
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Sydney Olympics 2000: An Overview

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INTRODUCTION

Sydney was chosen to be the site for the 2000 Olympic Games. Dope testing was regarded as an important factor in the success of the event. As the IOC accredited laboratory in the region, and being located in Sydney ASDTL was given the task of providing this service.

ASDTL's agreement with SOCOG to provide dope testing was negotiated and signed at the beginning of 1999 about one year after negotiations were begun. This agreement required the laboratory to be functional from the beginning of the Olympics to the end of the Paralympics. The period had the following critical dates:

- Olympic village opened 2nd September
- Opening ceremony 15th September
- Closing ceremony 1st October
- Paralympic village opened 11th October
- Opening ceremony 18th October
- Closing ceremony 29th October.

ASDTL had agreed that the laboratory would be Games ready from the second week of August 2000 with further staff training and practice undertaken until Olympic samples arrived. ASDTL was particularly busy during August because of increased out-of-competition demand from national, international and WADA sources, all of whom wanted to ensure athlete's drug free status for the Games.

ASDTL had responsibility for the analysis of samples during the Olympics. However all other doping control matters were organised through SOCOG. SOCOG were responsible for all sample collection venues, providing staff for collection of samples, equipment for

collecting both blood and urine samples, ensuring all protocols were correctly followed and transport of samples to the laboratory. During the period of the Games the IOC supervised all these processes and became the authority in control.

The ASDTL laboratory in Pymble, 20 minutes drive from the Olympic Stadium, was classified as a non-competition venue and SOCOG had responsibility to provide external security to vet all persons entering the car park and building. ASDTL was responsible to SOCOG to ensure internal security was of an acceptable standard.

TRANSPARENCY

Observation of anti-doping procedures included both the IOC Medical Commission (IOC MC) and representatives of the newly evolving World Anti-doping Agency (WADA) who acted as an Independent Observer team. Thus for the first time a watchdog was available to work with all parties to promote transparency and ensure there would be no suspicion of subterfuge which would cast a shadow on the dope testing process. WADA had two observers to report on the laboratory procedures. These observers were allowed to observe and assess any aspect of doping control in the laboratory. They could not interfere with any processes but since they were expert in the area they could, if needed, be involved in discussions. The report of the independent observers was subsequently published and is available on the WADA website.

All communication from the laboratory during the Games period was directly with the IOC Medical Commission and not to any other agency such as SOCOG. Thus all reports were only transmitted to Prince Alexandre de Merode the Chairman of the IOC MC. As agreed there was a simultaneous reporting of all results to WADA at their Sydney Olympic Games Office. There was no interaction with other parties such as Government or media.

EQUIPMENT

Equipment for the event was calculated on the basis that all results were to be completed within 24hours. Knowledge of factors such as run time, maintenance schedules, number of samples expected at any period, time associated with sample preparation and time required to analyse the data made it possible to estimate the number of machines required for each drug screen and production of expected turnaround times (TATs). The Table below shows the instrumentation requirements.

TABLE 1 – INSTRUMENTATION FOR SYDNEY OLYMPICS 2000

Instrument	Source
Benchtop Mass Spectrometers	
5 x MSD (5973)	SOCOG purchase
5 x MSD (5973)	SOCOG rental
5 x MSD (3 x 5970, 2x 5973)	ASDTL
5 x MSD (5973)	Agilent loan
1 x Finnigan GCQ	ASDTL
High Resolution Mass Spectrometers	
MAT95S	ASDTL
MAT 900	ASDTL
MAT 95XL	Finnigan rental
MAT 95	NARL
HPLC	
4 x Waters Alliance 2690	ASDTL and Waters rental
GC with NPD detection	
4 x HP	ASDTL and Agilent rental
Carbon Isotope Ratio	
2 x Finnigan	ASDTL and Finnigan rental
LCMS	
1 x Micromass Quatro	R&D section
Automated SPE	
5 x Gilson XL4	ASDTL and John Morris Scientific rental
3 x Gilson X222	ASDTL and John Morris Scientific rental
EPO Blood/urine analysis	
Bayer Advia	Bayer rental
DPC Immulite	
Dade Behring Nephalometer	
Fuji Camera	loan

SAMPLE NUMBERS

The number of competition samples received during the Olympic Games is shown in the Table 2. The actual sample numbers corresponded well with the figures predicted by SOCOG before the event. The unpredicted 30% increase in sample numbers due to out-of-competition samples arranged in the lead up to the Games required staff and equipment usage. The main impact was felt in the HRMS area where an extra research instrument (MAT900) had to be included into the screening process. If this instrument had not been available then

considerable delays would have been encountered and the required 24-48 hrs TAT would not have been possible.

TABLE 2 SAMPLE NUMBERS

Sample type	Number of samples		
	Total	Male	Female
Out-of-competition urine	437	267	170
Blood samples	310	166	144
Urine with blood samples	315	171	144
Competition samples	2148	1264	884
TOTAL	3210	1868	1342

STAFF

The number of trained staff required was calculated on the expected sample numbers. Shift numbers were allocated according to the predicted sample arrival time at the laboratory. Sample extraction occurred soon after arrival to allow the instruments time to complete the data collection for the analysis. Shifts were staggered and started every 2-4 hours. The number of staff per shift was dependent on the expected sample numbers predicted for each delivery. Staff numbers were a maximum at between midnight and 3am.

Whilst expert staff had to be present during all shifts. These experts were required to analyse data retrieved from the instruments soon after completion of data acquisition, usually by visual inspection of chromatograms by two analysts. These experts were also required to perform any confirmations of suspicious results to prove whether or not a banned substance was present. The final large number of positive results meant that the confirmation process required careful management of expert staff.

In total there were 90 staff utilised during the Games. Of these 42 were AGAL personnel with 20 from ASDTL. This also included the ASDTL research staff responsible for EPO and CIR during the Games. A further 27 AGAL staff were seconded from other sections such as

R&D, NARL and AGAL NSW. Their training into all aspects of the work – extraction, instrumental, data analysis and confirmation of positive results began 1998 as a series of one-month sessions. These short training sessions allowed the learning process to be staggered and to ensure no area within AGAL had excessive numbers of staff absent. Thus the work within all areas could be managed with minimum disruption.

The basic laboratory work such as sample preparation and extraction were tasks requiring only a limited amount of training and staff were recruited by Kelly Scientific (a staffing agency). The calibre of these technical staff was very high and training progressed very quickly and consisted of 3 weeks in August 2000 prior to beginning work on Games samples.

To ensure that the overall standard remained very high thirteen external expert staff were invited to work with our group. These people were seconded from anti-doping laboratories within Paris, Greece, Switzerland, U.K., Germany, Indonesia and experts in CIR from AGSO in Canberra. All these provided important expertise developed by considerable experience in their fields.

ANALYSIS RESULT REPORTING

Analysis within the laboratory tested for all the IOC banned substances for which tests were available. These substances were distributed between the classes banned by the IOC as set out in the IOC Olympic Movement Anti-doping Code January 2000.

Negative samples were reported between 4pm and 7pm each evening in time for the 10pm IOC MC meeting. These where possible represented samples received before 6pm the day before. Samples received after this time were included in the following days reports.

Positives were reported immediately upon:

- Confirmation and checking of data;
- Preparation of the documentation package including all chain of custody, sample information, sample preparation, instrumental data and analysis of data;
- Review of the documentation package by 2 members of IOC MC;
- The signing of the documentation package ASDTL Director and 2 members MC to indicate it contained justifiable data;
- The final report was then faxed to the Chairman, IOC MC.

IOC MC held hearings for positive cases on the same evening from 11pm after the IOC MC meeting.

IRMS CRITERIA

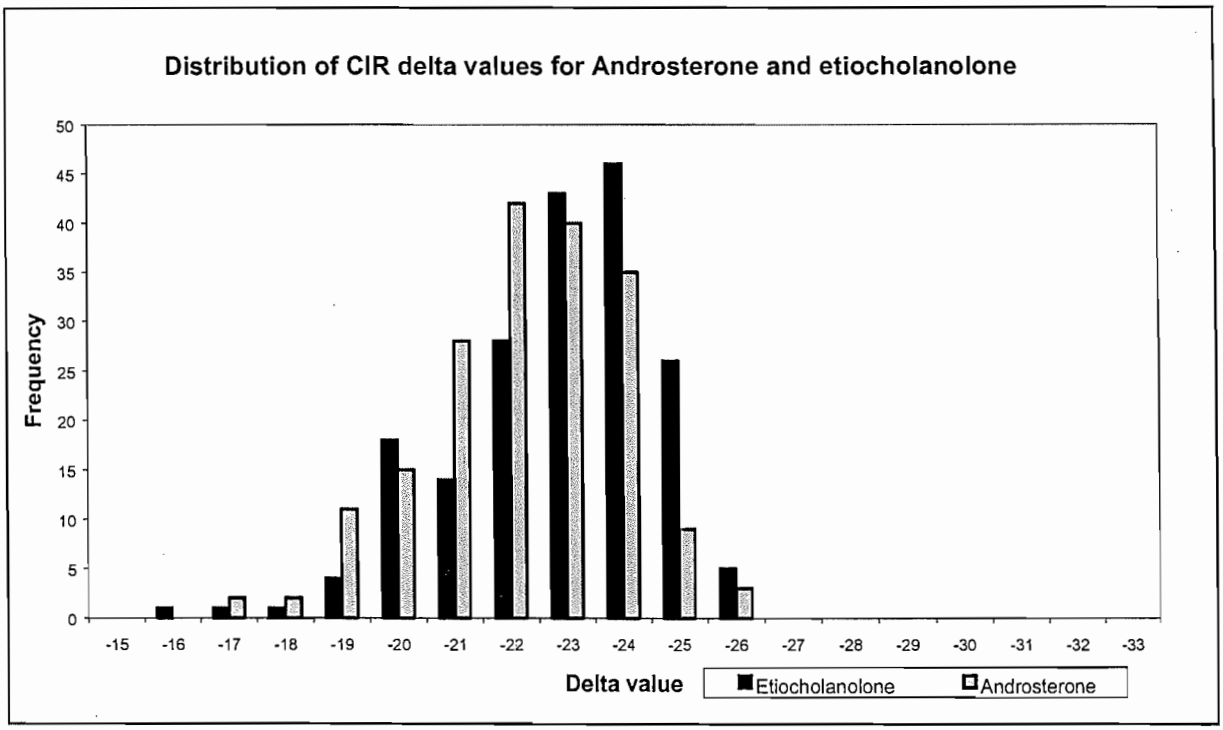
Routine steroid profiling data was used to decide if a sample would be forwarded to screening by CIR. The decision was based on:

- T/E > 3; androsterone and/or etiocholanolone concentration > 3000ng/mL;
- DHEA concentration > 100ng/mL;
- DHT parameters exceeded;
- epitestosterone concentration > 200ng/mL.

The CIR screening was based on measurement of both the absolute delta values for androsterone and etiocholanolone (underivatised) (value below δ –27.0 as positive) as well as their ratio to the endogenous marker 11-ketoetiocholanolone (value above 1.15 as positive).

Using the above rules no samples were suspicious (see Figure 1).

FIGURE 1



BLOOD/URINE PROTOCOL

Two models for testing for EPO had been developed and reviewed by the IOC. This allowed a protocol to be developed for declaring an athlete positive for EPO use. The protocol

required the use of both blood and urine tests. The blood test allowed the calculation of an ON or OFF score (1,2). The ON model score indicates a change in blood parameters, experienced while an individual is taking EPO and is distinguishable from normal EPO free blood parameters. The OFF model score indicates a change in blood parameters distinguishable from normal when an athlete has stopped taking EPO. The urine test (3) provided a quantitative measure for the basic/acidic glycoforms of EPO. RhEPO has a much more basic distribution of basic glycoforms to the normal population.

Declaration of a positive EPO result required that:

A the ON score > 2.75 for males and 2.55 for females; and

B the urinary EPO basic/acidic glycoforms >80%;

A sample could be reported as suspicious if:

C the OFF score >2.5 for males and 2.35 for females; or

D if only one of A or B are positive.

Samples with an ON score above 2.55 for males and 2.35 for females were screened by the urine assay.

In the case of suspicious results the sample is reported as suspicious to the Chairman of the IOC for possible follow up by the IOC and/or the International Federations.

The distribution of blood samples collected by sport is shown in Figure 2. The sports that were targeted were the ones whose athletes were believed most likely to use EPO. All samples collected for blood controls had the urine portion also analysed for all substances.

The distribution of the male and female EPO ON Model scores is shown in Figure 3. This shows that one female sample had parameters exceeding the cut-off levels we had set. This sample gave an ambiguous result in the urine test so the sample was declared negative.

Figure 4 shows the EPO OFF Model scores and this graph shows that there were 4 females and 3 males exceeding our limits.

Figure 5 shows the variation in basic isoforms. Two athletes –one male and one female – had basic/acidic values above 80%.

FIGURE 2

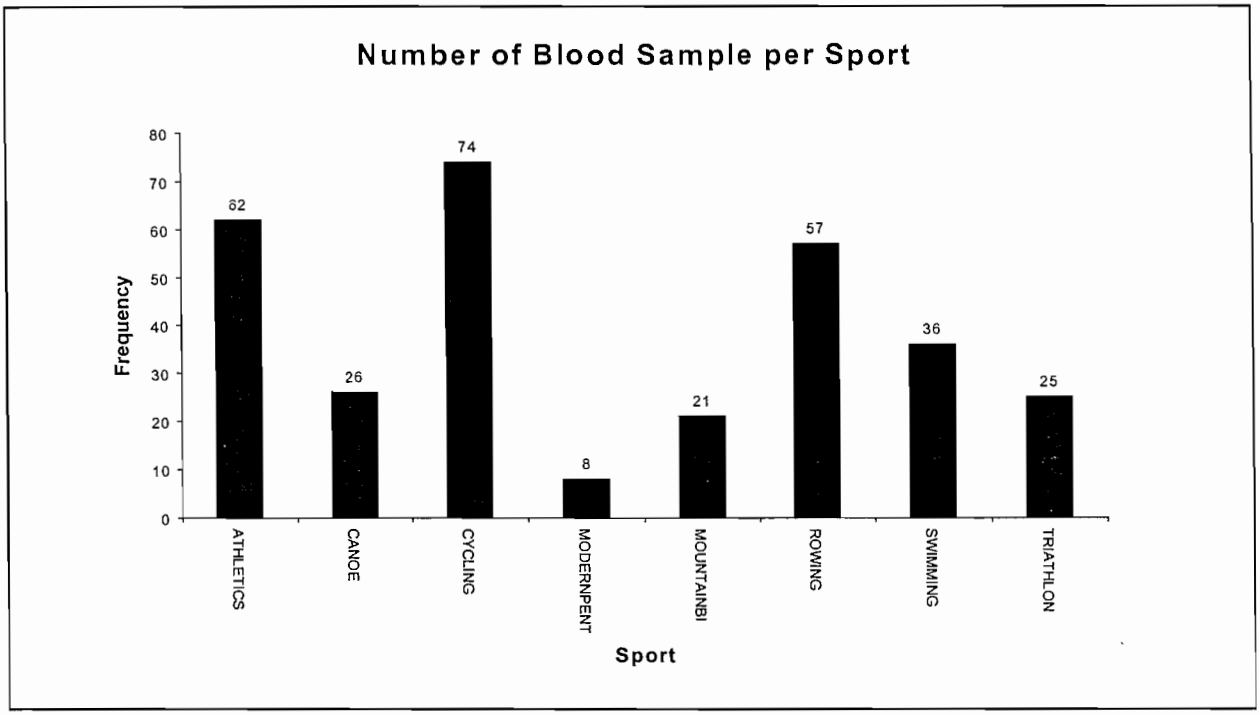


FIGURE 3

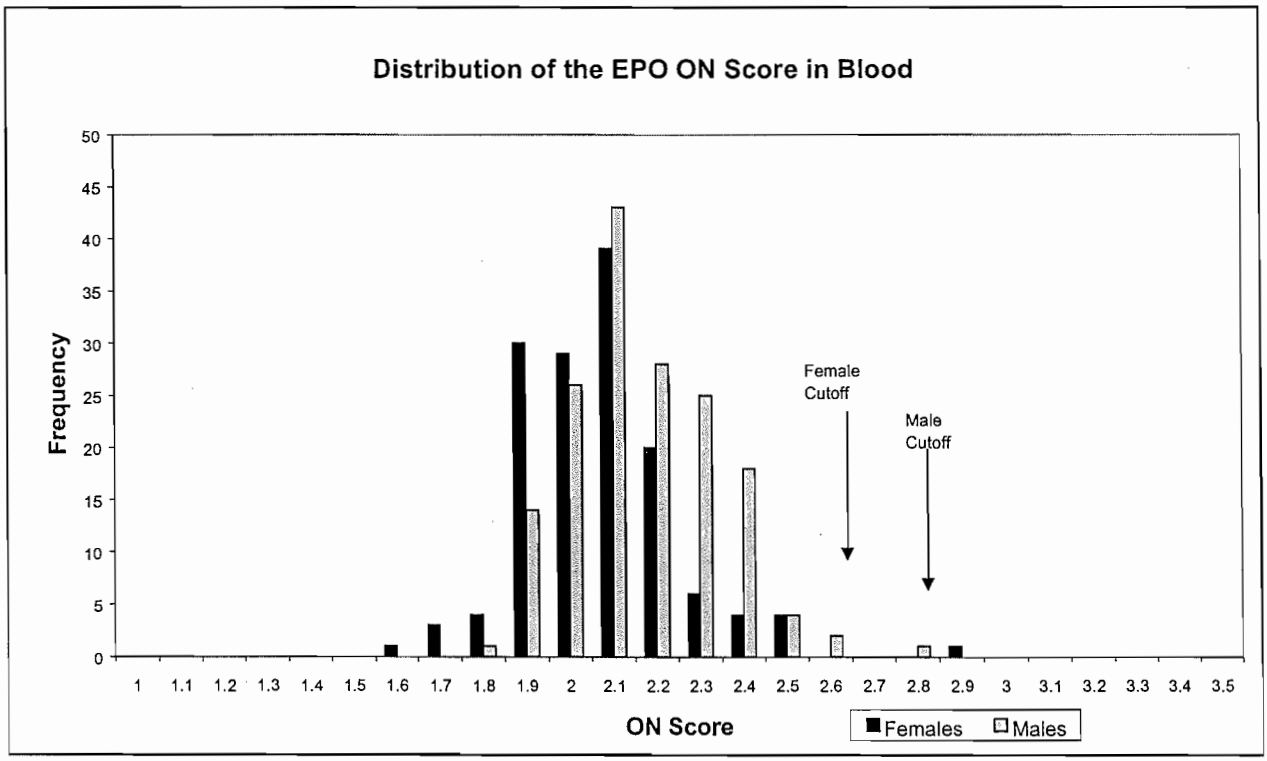


FIGURE 4

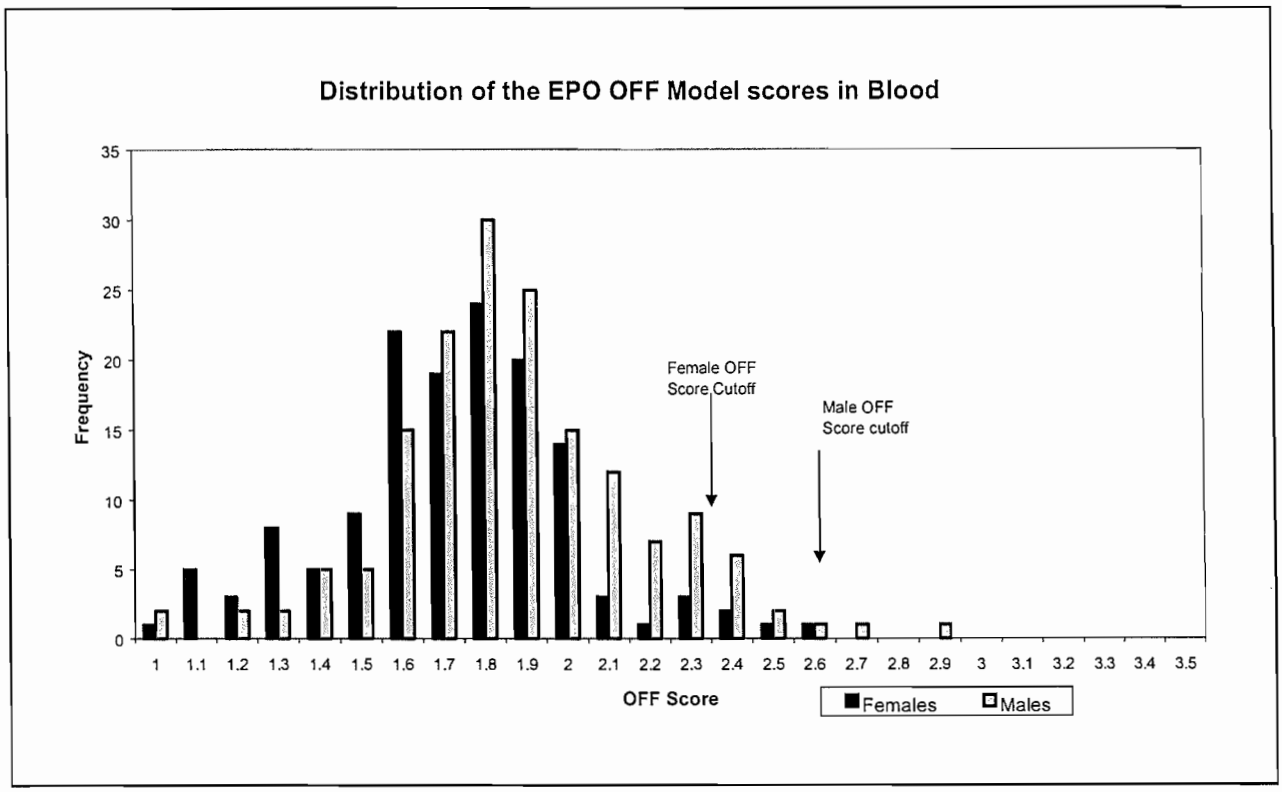
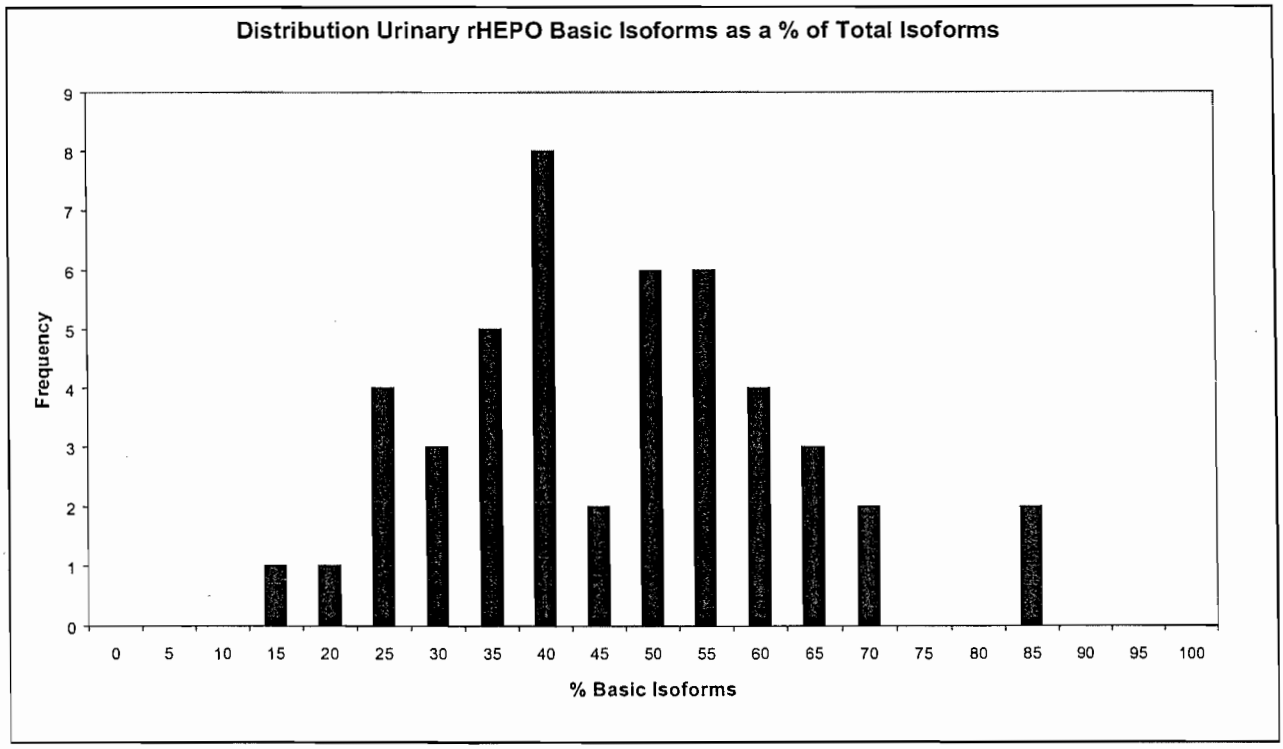


FIGURE 5



CONCLUSIONS

The final results for the Olympic testing programme are shown in Table 3. All six blind controls were correctly identified. Thirteen Salbutamol and two2 terbutaline results were reported and all these athletes had predeclared their use of b2-agonists on medical grounds. The eleven other positive results reported all led to sanction being imposed.

The results for the Paralympic Games testing is shown in Table 4. The three IPC controls were correctly identified. A number of medications had been approved by the Medical Advisory Panel and no action was taken. The remaining eleven positive results led to a sanction being imposed.

It is interesting to note that there was little evidence of EPO use during these Games but there was some indication that a number of athletes appear to have stopped EPO usage more than two weeks prior to their arrival in Sydney. The final outcome for the Olympic and Paralympic Games was a testing programme which was reviewed as satisfactory by WADA. The large number of positive results which led to sanctions are testimony to the fact that doping issues are taken seriously.

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TABLE 3 – RESULTS FOR THE OLYMPIC GAMES

Drug	B sample required	Type	Gymn.	Wtlift.	Wrest.	Row.	Athlet.	Total	Action Taken
Furosemide	**YES**	**Comp.**		**3**	**1**			**4**	**Sanction**
Nandrolone, norandrostenedione or norandrostenediol	**YES**	**3 Comp. 1 OOC**			**2**	**1**	**1 OOC**	**4**	**Sanction**
Pseudoephedrine	**YES**	**Comp.**	**1**					**1**	**Sanction**
Stanozolol	**YES**	**Comp.**		**1**			**1**	**2**	**Sanction**
Salbutamol	No	Comp.						13	Medication Allowed
Terbutaline	No	Comp.						3	Medication Allowed
Nikethamide	No	Comp.						1	IOC blind Control
Clostebol Clopamide	No	OOC						1	IOC blind Control
Clenbuterol	No	Comp.						1	IOC blind Control
Methandienone	No	Comp.						1	IOC blind Control
EPO	No	OOC						2	IOC blind Control

TABLE 4 – RESULTS FOR THE PARALYMPIC GAMES

Drug	B sample required	Type	Power-lifting	Athlet.	Swim.	Total	Action Taken
Hydrochlorothiazide	**YES**	**OOC**	**1**			**1**	**Sanction**
Methandienone, (Nandrolone)	**YES**	**OOC**	**1**			**1**	**Sanction**
Chlorthalidone	**YES**	**OOC**	**1**			**1**	**Sanction**
Stanozolol (nandrolone, T/E>6)	**YES**	**OOC**	**1**			**1**	**Sanction**
T/E > 6, CIR	**YES**	**OOC**	**1**			**1**	**Sanction**
Nandrolone (T/E>6)	**YES**	**OOC**	**1**			**1**	**Sanction**
Nandrolone	**YES**	**OOC**	**1**			**1**	**Sanction**
T/E > 6, CIR	**YES**	**OOC**	**1**			**1**	**Sanction**
Nandrolone	**YES**	**Comp.**		**1**		**1**	**Sanction**
Methandienone, nandrolone	**YES**	**Comp.**	**1**			**1**	**Sanction**
Methyltestosterone (T/E>6)	**YES**	**OOC**	**1**			**1**	**Sanction**
T/E>6	**No**	**OOC**	**1**			**1**	**Investigation**
Salbutamol	No	Comp.			2	2	Medication Allowed (MAP approval)
Hydrochlorothiazide, amiloride	No	OOC		1		1	Medication Allowed (MAP approval)
Hydrochlorothiazide, amiloride	No	Comp.		1		1	Medication Allowed
Furazabol	No	Comp.				1	IPC blind Control
Sotolol	No	Competition				1	IPC blind Control
Caffeine	No	Competition				1	IPC blind Control