SPORTS ANTI-DOPING RESEARCH FUNDING PROPOSAL

Development of Certified Reference Materials for the detection of doping with nandrolone

S. Westwood, L. Mackay and R. Kazlauskas

NATIONAL ANALYTICAL REFERENCE LABORATORY
AUSTRALIAN GOVERNMENT ANALYTICAL LABORATORIES
1 Suakin St, Pymble, NSW, 2073 Australia

SPORTS ANTI-DOPING RESEARCH FUNDING PROPOSAL

Application Form and Information Requirements

Organisational Details

Legal name of organisation	**Commonwealth of Australia, Department of Industry, Tourism and Resources**
Short name or trading name	**Australian Government Analytical Laboratories**

Type of organisation

Non-profit organisation	Regional organisation
For profit organisation	Educational institution
Registered charity/charitable organisation	Aboriginal or Torres Strait Islander organisation
Health institution	X Government
Community group	Private individual

Postal address

Street name & number/PO box	1 Suakin St.				
Suburb/Town	Pymble				
City	Sydney	State/Territory	NSW	Postcode	2073

Nominated contact for project/program

Title	Dr
First name	Steven
Last name	Westwood
Position	Leader, Reference Materials Team, National Analytical Reference Laboratory
Phone	02 94490111
Facsimile	02 94491653
Email address	steven.westwood@agal.gov.au

Organisation Identification

Australian Business Number (ABN) or Australian Company Number (ACN)

5	1	8	3	5	4	3	0	4	7	9	0	0	2

Is the organisation

GST registered?	Yes	x	No	
Incorporated?	Yes		No	x

If yes, please provide the incorporation number and year of incorporation

Incorporation number											
Date of incorporation											

Purpose/objective/mission statement of organisation (5 lines max)

The Australian Government Analytical Laboratories (AGAL) is the Australian Government's principal agency for the provision of analytical services in chemistry, microbiology, and materials and building science

Information requirements

The following information must be provided with this application

1. Details of any ethical consideration for the project. – **Include a copy of National Health and Medical Research Council approved ethical committee application form, informed consent form, and documentation of the ethical approval process.** ***See attached papers***
2. A detailed budget for the project. This should include: – **A detailed cost item breakdown;** – **Detailes of where the funds will be spent; and** – **Details of any other capital or in-kind support secured for the project.** ***See attached papers***
3. Consultation and/or collaboration arrangements. – **Identify the International Olympic Committee accredited laboratory(ies) that you will communicate or collaborate with to ensure that the new or modified detection protocols and methodologies developed by your research can be implemented by IOC accredited laboratories.** ***The National Analytical Reference Laboratory is the applicant. NARL will work closely with the Australian Sports Drug Testing Laboratory during this project. It is anticipated that an ongoing program will be developed that will result in the production of a suite of urine-matrix reference materials for all doping laboratories.***
4. Project summary, suitable for publication (maximum 1000 words) ***See attached papers***
5. Project description. – **This should focus on the expected outcome of the project and the selection criteria (max 5 pages).** ***See attached papers***
6. Project timetable, including proposed milestones. ***See attached papers***
7. Project management plan, including reporting and evaluation plans. ***See attached papers***
8. Other enclosures. **a. Curriculum vitae of principal investigator with 10 relevant, recent publications** **b. Curriculum vitae of main collaborating investigators with 5 relevant, recent publications** **c. List of literature relevant to the project (max 10 publications)** ***See attached papers***

DECLARATION: I declare that, to the best of my knowledge, the information provided in this application is true and complete, and that I have read, understand, and agree to comply with the Guidelines for Applicants.

Signature of CEO or equivalent office holder:

Date:

Project Title

Development of Certified Reference Materials for the detection of doping with nandrolone

1. Ethical Considerations

None, as no drug administrations are proposed.
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2. Budget - Request

Project budget	
Expense category	**Amount (AUD)**
Year 2004	
Salary, scientific personnel:	
8.5% of section leader + oncosts	**9,000**
17% of senior research scientists + oncosts	**14,700**
17% of scientific officers + oncosts	**12,000**
17% of technical officers + oncosts	**10,500**
Equipment	
Operating costs – inc. depreciation, maintenance	**12,500**
Consumables/Standards:	
General reagents and consumables	**2,000**
Steroid starting materials	**3,500**
Other direct costs and overheads	**35,800**
Total budget	**100,000**

Note:
The project is complementary to a project to produce urine-matrix reference materials for the same purpose that is being funded by WADA to the extent of US$ 250,000.

BUDGET JUSTIFICATION

A project to develop both solution-based and urine-matrix reference materials for use in the detection of nandrolone doping was commenced in September 2003 on the basis of partial funding by the World Anti-Doping Agency WADA. A contract between WADA and AGAL has been signed for the period to June 2004 under which WADA supplies US $ 150,000 to AGAL to undertake the first year of the work. Provisions are included in the contract for WADA to supply an additional US $ 100,000 to complete the work in 2004/05, provided that the reports on work undertaken in the first year and supplied to WADA are satisfactory and that AGAL is prepared to proceed with the contract.

Since the drawing up of that contract, however, the Australian currency has increased dramatically in value in comparison to the US dollar, meaning that the US$ funding provided by WADA has decreased markedly in real terms for AGAL in addressing its project costs. The budget for the project assumed an exchange rate US $ 0.60 for the AUD, and was developed when the exchange rate was below US $0.55 per AUD. Now the latter is valued at closer to US $ 0.78, a change of about 30%, representing a lowering of funds available to the project by AUD $ 75,000. The result is that the project now cannot be being continued in its complete form into the 2004/05 financial year unless funding is provided from another source for at least part of the work originally to be financed by WADA.

The discontinuation of the project would represent a most regrettable outcome for the Australian sporting and drug detection community. The successful completion of the project would place Australia at the forefront of such research and further enhance our country's reputation as a world leader in the detection of the use of performance-enhancing drugs in sport and their elimination from international competition. Because of the project's direct links with WADA, the use of the project outcomes by IOC laboratories around the world would be guaranteed, meaning that the transformation of the research results into positive action would be immediate and most important. The availability of suitable certified reference materials would strengthen the possibility of successful prosecutions being undertaken for the unauthorised use of nandrolone to enhance sporting performance and help protect sporting organisations from legal action based on their suspension of athletes on drug usage grounds.

It is therefore requested that the ADRP program provide a sum of $100,000 to AGAL for work to be conducted in this area for 2004. This particular section of the work to be withdrawn from the WADA project and funded separately is that associated with developing, characterising and distributing solution-based CRMs. The funding will then complement that of WADA to ensure that suitable reference materials for the detection of nandrolone use are available to sports drugs laboratories both within Australia and overseas. It will also provide a platform for the development of other reference materials for other prohibited drugs in the future.

Project Summary

Development of Certified Reference Materials for the detection of doping with nandrolone

The aim of the project is to produce standard solution Certified Reference Materials (CRMs) for the marker metabolites of key anabolic steroids. The CRMs will be used to ensure all doping control laboratories operating in accordance with the WADA Anti-Doping Code [1] can report the presence of these prohibited substances in a uniform reliable way and that they meet the Minimum Required Performance Limit (MRPL) at which they are required to operate.[2] A sum of $ 100,000 over one year is sought from the ADRP programme to support this work. The project is complementary to a larger project to produce urine-based CRMs for similar purposes. This larger project is being funded to the extent of USD 250,000 by the World Anti-Doping Agency (WADA) whose involvement will guarantee the effective dissemination of the results.

Although standard solution CRMs, prepared and characterised in a metrologically rigorous manner are the ideal benchmarking tools for these tests there are none currently available for the detection of anabolic steroids, nor indeed are any urine-matrix CRMs available that are relevant to testing for doping with steroids. This project will commence investigation into this very important area, with the expectation that an ongoing program will be developed that will result in the production of a suite of both solution and urine-matrix CRMs for doping laboratories. The first stage, which forms the basis of this application, is to establish CRMs in a simple solvent matrix. This work will then be expanded under the WADA funding to develop urine-based CRMs.

Demonstrating the capability to detecte banned steroids is of course a key component of the technical requirements for the accreditation by WADA of doping analysis laboratories.[2] The availability of appropriate solution CRMs will assist them to establish compliance with the requirements of ISO/IEC 17025 [3] as well as to meet the requirements of the WADA Anti-Doping Code. The CRMs are intended for benchmarking current testing methodology as well as allowing laboratories to more readily detect and address potential bias in their analytical methods. Their use in testing and in the confirmation of potential positives will result in the following:

- The results obtained on nandrolone detection will be endowed with greater confidence and increased intercomparability.
- Most importantly, markedly more robust arguments will be available to regulatory bodies when justifying their results under aggressive legal scrutiny.
- Research into new or improved methods for the qualitative and quantitative detection of nandrolone doping will be facilitated.
- The inclusion of the CRMs in routine testing procedures will strengthen the metrological traceability of results obtained by doping laboratories to the International System of Units (SI) and assist in the estimation of the measurement uncertainty of their results.

Project Outputs:

- Standard solutions, packaged into ampoules, certified for use in the detection of the marker metabolites of the most commonly encountered banned steroids. They will be produced for the steroids (marker metabolite in parentheses) nandrolone (19-norandrosterone) stanozolol (3´-hydroxystanozolol), methyltestosterone (17a-methyl-5a-androstane-3a,17ß-diol) and dianabol (epimetendiol).
- Distribution of the solution CRMs to selected doping laboratories for a round-robin analysis.

This output will complement the wider, WADA-funded project, whose outputs will be:

1. A development study assessing the feasibility of production and characterisation of a urine-matrix CRM specifically for detection of nandrolone doping in a form suitable for testing laboratories.

2. If the development study is successful, production and certification of a urine-matrix material containing a certified level of the nandrolone metabolite 19-norandrosterone. The material will be spiked with 19-norandrosterone as its glucuronide derivative, the predominant form in which it is found in urine. It will be certified for equivalence to free 19-norandrosterone at 2 ng/mL, the decision level for positive results in male athletes.

3. Distribution of the urine-matrix CRM to doping laboratories for round-robin analysis.

Background & Discussion

An analysis for doping with anabolic steroidal agents requires the detection of their marker metabolites in urine at part per billion (ng/ml) levels.[2] In the case of nandrolone there is an additional requirement to quantitate the amount of metabolite present. [4]

It is a condition for IOC accreditation that a laboratory can demonstrate its technical capacity to undertake these analyses using an appropriate Quality Assurance system. At present testing laboratories have had to develop their own protocols for monitoring their capabilities and their routine performance of these critical assays.

Appropriate standard solution CRMs, prepared and characterised in a metrologically rigorous manner,[5, 6] are the ideal benchmarking tools for these tests. Their availability would make a major contribution to establishing traceability linkages both between testing laboratories and to the SI, to increasing the confidence in the results obtained by individual laboratories and to reducing the potential for the successful challenge of positive results. They would also assist research into new or improved methods for the qualitative and quantitative detection of these compounds.

Our research group has a demonstrated, accredited capability in all aspects of the production, analysis and certification of pure substance reference materials of anabolic steroids and their metabolites in accordance with international best practice. As a result we are uniquely qualified to address the whole range of technical issues that are required in order to ensure that CRMs produced by this project are fit for their intended purpose.

Production of standard solution CRMs

Pure substance CRMs of all the metabolites required have been produced by the Reference Material team of the Australian Government Analytical Laboratories' National Analytical Reference Laboratory (NARL).[7] These materials are already widely used by WADA-accredited doping analysis laboratories as reference standards. Standard solutions will be prepared from these materials in a metrologically rigorous manner and the gravimetric concentrations will be confirmed and certified using at least one independent method (eg. isotope dilution GC-MS, GC-FID). As required for a CRM, uncertainty estimates will be included for all certified concentrations. The solution stability of the candidate materials will be assessed in a range of solvents in order to develop the optimum system that gives both acceptable storage stability and is suitable for the intended end use of the standard.

Standard solution steroid CRMs will have many potential applications. They can be used to assess the performance of the various screening methods (GC-MS, LC-MS, HRMS, GC/LC-MSMS) used to detect steroid abuse. Experience has shown that even when using a defined the quantitation estimates for trace metabolites can fluctuate due to a variety of factors. These include the tuning, maintenance and age of the MS detector, interference by co-eluting impurities and GC-column performance. This difference can be even more marked when results are compared for the same sample obtained using different assay techniques. Having standard solutions available with certified steroid profiles will allow for accurate monitoring of operational bias in the results obtained from a specific analysis run and will permit an analyst to flag potential positives with greater confidence. The CRMs will also be of use in confirmation assays, for essentially similar reasons. Their role in this case would be as positive controls allowing any bias in the confirmation methodology to be assessed in a statistically robust fashion.

Production of a urine-matrix CRM

Although a solution CRM will be useful and have many applications, a urine-matrix CRM equivalent to the true analytical challenge presented to testing laboratories will be even more valuable. The production of a matrix CRM of this type in a metrologically-rigorous manner is a much greater technical challenge[4] and is being undertaken with the more extensive WADA funding. The development phase of the project, would investigate the following:

- evaluating the preferred storage protocol (freezing, freeze-drying, etc)
- characterising the steroid concentrations of a pooled unspiked urine
- developing and validating an appropriate gravimetric spiking protocol
- assessing the stability of both spiked and blank urine
- development of a reference method for the analysis of 19-norandrosterone in urine.

Note that the aim with the matrix CRM will be to prepare the material by spiking with the glucuronide metabolite of the steroid rather than the free compound. This is the predominant form in which the material is found normally in urine.

Once initial studies confirm the viability of producing a urine-matrix CRM the second phase, rigorous certification of the 19-norandrosterone concentration, will be undertaken. This phase of the project poses a major technical challenge. It will require the development of a high-accuracy reference method to determine the absolute concentration of 19-norandrosterone. An uncertainty estimate for the assigned value would be included. Possible approaches to certification of the CRM would be judicious use of LC-MS, GC-MS or high resolution mass spectrometry (HRMS) assays using the technique of isotope dilution mass spectrometry to establish the concentration.[5] Full homogeneity testing of the material will also be carried out.

The certification of the CRM should be carried out in a metrologically-rigorous, transparent manner because the value assigned to the CRM will become a baseline value in establishing traceability linkages of the results obtained by doping laboratories. It will also be of critical importance in the assessment by laboratories of the measurement uncertainty associated with their screening and confirmation protocols. The NARL Primary Methods group will carry out this phase of the project. They have an established record of successful participation in international metrological comparison studies on trace level organic analysis using isotope dilution MS methodology.[6]

It is anticipated that, if a suitable candidate matrix CRM can be produced, it will be included in a round-robin analysis by IOC/WADA accredited laboratories to allow comparison of the value assigned by the reference method with the results obtained by expert laboratories.

References

1. WADA Anti-Doping Code (2003).
2. ISO/IEC17025 (1999): General requirements for the competence of testing and calibration laboratories.
3. ISO Guide 34:2000: General requirements for the competence of reference material producers.
4. J. Pauwels et al; “Evaluation of Uncertainty of Reference Materials”, *Proceedings of Eurachem Workshop on Evaluation of Uncertainty in Analytical Chemistry*, 1999.
5. P. De Bievre and H.S. Peiser; “Basic equations and uncertainties in isotope dilution mass spectrometry for traceability to SI of values obtained by this primary method” *Fresenius J. Anal. Chem* ., **359** (1997), 523-525
6. See NARL results for CCQM-K5, CCQM-K6, CCQM-K21 reported on BIPM Key Comparisons Data Base, Appendix B (http://kcdb.bipm.fr/BIPM-KCDB/AppendixB/)

Research Plan:

The following objectives will need to be met:

1. Establishment of CRM requirements

   A literature review and consultation with key stakeholders and testing laboratories active in the area will be undertaken to establish the target parameters for the solution and matrix CRMs, preferred amount for supply and preferred format of the matrix. In particular we would liaise with the EU-funded ALADIN consortium and aim to harmonise our production protocols with theirs and ensure there is no duplication of effort.

2. Preparation of the candidate CRMs

3. Standard solutions will be prepared in a controlled gravimetric manner and the effect of ampouling on the assigned concentrations will be checked by a quantitative chromatographic methods. Homogeneity and stability studies on the candidate materials will also be undertaken, and the effect of various solvents on the long-term stability of the dissolved analytes will be examined.

4. Certification of the steroid ratios and absolute concentrations.

   The development studies if successful will demonstrate that the steroid profiles of the candidate materials are fit for their intended purpose and that the solutions and/or urine matrices are sufficiently robust to justify their characterisation as CRMs. Certification of the materials will only be undertaken if the development studies indicate the candidate materials are suitable for the end-user requirements. When completed, the CRMs will have the property values for their concentrations determined with an accompanying uncertainty estimate.

5. Storage and distribution of the materials

   The CRMs produced as a result of the work will be added to the existing collection of NARL anabolic steroid reference materials. They will be sold on request to approved laboratories, with the price to the endusers reflecting the cost of their storage, ongoing stability and QC analysis and distribution, but not production.

Resources and Equipment:

We have access to the following capital equipment required to undertake the project:

1. Within NARL

- GC-MS (Agilent 5973 MSD, Saturn 2000 Ion trap)
- HRMS (Finnigan MAT-95)
- Bulk handling/filtration/cold storage facilities for solution and matrix CRMs
- Semi-automated ampouling apparatus

2. Within ASDTL

- GC-MSD (Agilent 5973 MSD, GCQ Finnigan Ion Trap)
- HRMS (Finnigan MAT-95)
- LC-HRMS (Finnigan MAT-90)

Project management

A project management team has been formed, consisting of

Dr Steven Westwood (chair)

Dr Lindsey Mackay

Dr Ray Kazlauskas

This team will meet monthly to manage the project against the above research plan.

- **CV of PRINCIPAL INVESTIGATOR**

NAME: Dr. Steven William WESTWOOD

ADDRESS: National Analytical Reference Laboratory,
Australian Govt. Analytical Laboratories,
PO Box 385
Pymble N.S.W. 2073

CURRENT POSITION: Team Leader, Reference Materials,
National Analytical Reference Laboratory

CURRENT EMPLOYER: Australian Government Analytical Laboratories

Tertiary Education

First Degree (1977-81): B. Sc. Hons (First class) in Organic Chemistry, University of Adelaide

Second Degree (1981-84): Ph. D. in Organic Chemistry, University of Cambridge

Career Highlights

1984 PhD in Organic Chemistry from University of Cambridge, U.K, working with Professor Sir Alan Battersby, FRS.

1988 Queen Elizabeth II National Research Fellow at Research School of Chemistry, ANU.

1997-99 Lead role in the synthesis and characterisation of anabolic steroid reference materials for use in the Sydney 2000 Olympics drug testing program and world-wide by other IOC-accredited laboratories.

1999 Lead role in the development, documentation and implementation of an in-house Quality System for the production of Certified Reference Materials and accreditation in to ISO 34.

2000^{+} Australian delegate to the International Standards Organisation Reference Materials Committee (ISO-REMCO, elected vice-chairman for 2004).

Employment History

(i) ***Current position***

Position: Team Leader, Reference Materials,
National Analytical Reference Laboratory, AGAL

Duties I am the team leader for a group responsible for the preparation, characterisation, certification and provision of a range of pure organic substance reference materials for use in three major areas of interest: veterinary medicines & agrochemicals, illicit drugs and anabolic steroids. I was directly responsible for preparing and certifying a range of anabolic steroids for use by the Australian Sports Drug Testing Laboratory in their assays for these banned substances. These materials are now in use worldwide by IOC-accredited drug testing laboratories. The work involved all aspects of the synthesis, purification and characterisation of the materials, both in-house and under external contract, in accordance with accreditation to ISO Guide 34 for the production of Reference Materials.

I am currently the Australian delegate to the International Standards Organisation Reference Materials Committee (ISO-REMCO) and am the vice-chairman for 2004.

(i) Prior employment

1991-96:	Research Scientist in immunochemistry division of Biotech Australia
1989-90:	Lecturer in Organic Chemistry (fixed-contract), School of Chemistry, University of Sydney.
1987-88:	QEII Research Fellow at the R.S.C., A.N.U.
1986:	Post-doctoral Fellow, Research School of Chemistry, A. N. U., working with Professor Athel Beckwith.
1985:	Post-doctoral Research Associate, University of Wisconsin, working with Professor Ed Vedejs.

RECENT PUBLICATIONS & PRESENTATIONS:

Steven Westwood, Bruce Noble and Christie Moule, "Preparation and Characterisation of Steroid Reference Materials"; *Proceedings of the 15th Australian International Symposium on Analytical Science* (1999)

Steven Westwood, Bruce Noble and Christie Moule, "Synthesis and characterisation of steroid metabolites for use as analytical Reference Materials"; *Proceedings of the 17th Cologne Workshop on Dope Analysis*, (1999) p. 181.

S. Westwood, D. Hancock, C. Moule, B. Noble and S. Starling, "Progress in the Preparation of Steroid Reference Materials & Certified Reference Materials"; *Proceedings of the 18th Cologne Workshop on Dope Analysis*, (2000)

G. Trout, R. Kazlauskas and S. Westwood; "The Role of Reference Standards in the Sydney 2000 Olympic Games Drug Testing Program"; *CITAC Newsletter* **2001**

B. King and S. Westwood: "GC-FID as a Primary Method for Establishing the Purity of Organic CRMs Used for Drugs in Sport Analysis", *Fresenius J. Anal. Chem.*, **2001**, *370*, 194

S. Westwood; "The Role of Reference Materials in Quantifying Measurement Uncertainty" Proceedings of NATA Reference Materials Symposium, Melbourne (December 2001)
S. Westwood, D. Hancock and P. Harvey; "Characterisation of the impurity profile of a tributyltin chloride analytical standard" (submission to the Consultative Committee on Amount of Substance (CCQM) Organic Working Group, Pilot International Intercomparison Study P-20a, April 2002)

S. Westwood, P. Harvey and R. O'Brien; "Characterisation of substances for Chemical Purity – *ortho* Xylene" (submission to the Consultative Committee on Amount of Substance (CCQM) Organic Working Group, Pilot International Intercomparison Study P-20b, November 2002)

S. Westwood, D. Hancock, B. King, H. Wang, J. Makrynikolas and S. Starling, "Stability Trials of Anabolic Steroid Reference Materials"; *Proceedings of the 19th Cologne Workshop on Dope Analysis*, (2001)

T. Kuuranne, T. Kotiaho, S. Pedersen, K. Rasmussen, A. Leinonen, S. Westwood and R. Kostiainen; "Liquid chromatographic/mass spectrometric screening method for selected anabolic steroid glucuronides in biological samples"; *J. Mass Spectrom.*, **2003**, *38*, 16

S. Westwood, B. King and B. Noble; "Implementation of ISO Guide 34 Accreditation for Reference Material Production"; *Accred. and Quality Assurance*, **2003**, *8*, 424-427

D. Hibbert and S. Westwood; "The external review committee on pure reference materials at the National Analytical Reference Laboratory" *Accred. and Quality Assurance*, **2003**, *8*, 434-435

S. Westwood, S. Davies and G. Tarrant, "Preparation of Certified Reference Materials for use in doping analysis for steroid prohormones and 19-nor steroids"; *Proceedings of the 21st Cologne Workshop on Dope Analysis*, (2003)

S. Westwood, S. Davies, H. Wang, P. Harvey and B. King; "Developments in the Certification of Pure Organic Substance CRMs*", 9th Symposium on Biological and Environmental Reference Materials* (Berlin, 2003*)*.

S. Westwood and L. Besley; " A Producer's View of the Production and Applications of Pure Substance Reference Materials for Sports Drug Testing *", 9th Symposium on Biological and Environmental Reference Materials* (Berlin, 2003*)*.

ATTACHMENT B: CVs of COLLABORATING INVESTIGATORS

Dr Ray Kazlauskas

Address: **Australian Government Analytical Laboratories**,
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N.S.W. Australia.
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QUALIFICATIONS:

B.Sc. 1st Class Honours, University of Sydney. 1968.
Ph.D. University of Sydney, 1972.
Post Doctoral work with Professor A.R. Battersby, University Chemical Laboratory,

EMPLOYMENT HISTORY:

1988-present	Director, Australian Sports Drug Testing Laboratories, AGAL, Pymble
1986-1988	Research and Development, Australian Government Analytical Laboratories, Pymble.
1982-1986	Senior Research Officer, Department of Pharmacology, University of Sydney.
1981-1982	Visiting Fellow, Research School of Chemistry, A.N.U.
1973-1981	Senior Scientist, Roche Research Institute of Marine Pharmacology

RESPONSIBILITIES:

Management of the **Australian Sports Drug Testing Laboratory** (IOC accredited since 1990) including strategic planning, customer service and marketing, achievement of budgets and other corporate objectives of the ongoing dope testing program; liaison with overseas IOC laboratories and Governments in research in Drugs in Sport.

COMMITTEES:
SOCOG - IOC Coordination Commission - Doping Control Working Group
FINA Taskforce Committee member 1998
IOC Medical Commission, Doping and Biochemistry Subcommission
WAADS Executive committee.

RECENT PUBLICATIONS:

Trout G. J. and Kazlauskas R. (2004) Sports drug testing – an analyst's perspective. Chemical Society Reviews. 33:1-13.

Goebel C., Trout G. J., Kazlauskas R. (2004) Rapid screening method for diuretics in doping control using automated solid phase extraction and liquid chromatography-electrospray mass spectrometry. Analytica Chimica Acta 502:65-74.

Kazlauskas, R. (2002), Analysing the Olympic Games: A case study within the Anti-Doping Programme: An Overview. *Clin. Biochemist Reviews*, 2002; 23(ii): 35

Kazlauskas, R., Howe, C. and Trout, G. (2002), Strategies for rhEPO detection in sport. *Clin. J. Sports Med*. 12(4):2002;229-235.

Gore C. J., Parisotto R., Ashenden M. J., Stray-Gundersen J., Sharpe K., Hopkins W., Emslie K., Howe C., Trout G. J., Kazlauskas R., Hahn A. G. (2003). Second generation blood tests to detect erythropoietin abuse in athletes. Haematologica 88:333-344.

Trout, G., Kazlauskas R. and Westwood, S. (2001). The Role of Reference Standards in the Sydney 2000 Olympic Games Drug Testing Program. *CITAC Newsletter*.

Parisotto, R., Wu, M., Ashinton, M.J., Emslie, K.R., Gore, C.J., Howe, C., Kazlauskas, R., Sharpe, K., Trout, G.J., Xie, M. and Hahn, A.G. (2001). Detection of recombinant human erythopoietin abuse in athletes utilising markers of altered erythropoiesis. *Haematologica* 86: 128-137.

Kazlauskas, R. and Trout, G. (2000). Drugs in sports: analytical trends**.** *Ther. Drug Monit*. 22:103-109.

Corrigan, B. and Kazlauskas, R. (2000). Drug testing at the Sydney Olympics. *Med. J. Austral*. 173:312-313.

Allan, R.D., Dickenson, H.,W., Johnston, G.A., Kazlauskas., R., and Mewett, K.N. (1997). Structural analogues of ZAPA as GABA agonists. *Neurochem. Int*. 30:583-59.

Dr. Lindsey Gillian Mackay,

Team Leader, Primary Methods Group
National Analytical Reference Laboratory, Australian Govt. Analytical Laboratories
1 Suakin Street, Pymble, NSW 2073
Australia.

Academic Qualifications

1988 BSc. in Chemistry, University of Auckland, New Zealand.

1989 MSc. in Chemistry, first class honours, University of Auckland.

1993 PhD. in Chemistry, University of Cambridge, England.

Research Experience

Oct 1990-Dec 1993

Research towards a PhD in Organic Chemistry, University of Cambridge with Prof. J. K. M. Sanders titled "Porphyrin-Based Synthetic Enzymes". Synthesis, binding studies and catalytic studies on porphyrin-based macromolecular hosts utilising NMR and GC/FID.

Jan 1994-August 1995

Postdoctoral Research Fellow in the Department of Organic Chemistry, University of Sydney working on recognition abilities of chiral clefts.

Sep 1995-Nov 1996

Professional Officer in the R&D Section of the Australian
Government Analytical Laboratories (AGAL). Responsible for method development under AGAL's Public Interest Program and method development for commercial clients.

Dec 1996-Sep 1998

Senior Chemist in the R&D Section of AGAL. Responsible for management of AGAL's Product Development projects, management of Public Interest method development projects and for method development of HPLC and LC/MS methods for commercial clients.

Oct 1998-present
Team Leader, Primary Methods Team, National Analytical Reference Laboratory, AGAL.
Responsible for a team of scientists developing high accuracy trace organic and trace inorganic analysis methods using primary methodology, principally isotope dilution mass spectrometry techniques. This work involves participation in international metrological intercomparisons to demonstrate the equivalence of NARL's reference measurement capability and the use of this capability in the certification of matrix reference materials.

Recent Publications

1) L.G. Mackay, C.P. Taylor, R.B. Myors, R. Hearn and B. King, High accuracy analysis by isotope dilution mass spectrometry using an iterative exact matching approach, *Accred. Qual. Assur.*, 2003, **8**, 191-194.
2) L. Johnston, L. Mackay and M. Croft, Determination of quinolones and fluoroquinolones in fish tissue and seafood by high-performance liquid chromatography with electrospray ionisation tandem mass spectrometric detection, *J. Chromatogr. A*, 2002, **982**, 97-109.
3) L.G. Mackay and B. King, International CCQM and APMP Activities in Chemical Metrology, *Proceedings of the Metrology Society of Australia 4th Biennial Conference*, 2001, 13-16.
4) E.R. Vickers, C. Goebel, L.E. Mather, L.G. Mackay and R.J. Wells, High-performance liquid chromatography determination of bradykinin in saliva: a critical review and a new method, *J. Chromatogr. B*, 2001, **755**,101-110.
6) J.P. Mackay, J.M. Matthews, R.D. Winefield, L.G. Mackay, R.G. Haverkamp and M.D. Templeton, The hydrophobin EAS is largely unstructured in solution and functions by forming amyloid-like structures, *Structure*, 2001, **9**, 83-91.
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