## Tribunal Arbitral du Sport



## Court of Arbitration for Sport

Arbitration CAS 2002/A/370 L. / International Olympic Committee (IOC), award of 29 November 2002\*

Panel: Mr Peter Leaver QC (England), President; Ms Barbara Shycoff (United States), Mr Dirk-Reiner Martens (Germany)

Cross Country Skiing/Olympic Games Doping (darbepoetin) Reliability of the testing method

- 1. Although darbepoetin is not specifically listed as a prohibited substance in the Olympic Movement Anti-Doping Code ("OMAC"), it is an analogue or mimetic of erythropoietin which is recombinant EPO in that it is an artificial substance which is not naturally produced by the human body unlike natural EPO. Therefore it is a prohibited substance. In accordance with the OMAC, its use is permitted only to treat insulin-dependent diabetes and even then, only if written notification has been given prior to the particular competition by an endocrinologist or the team physician. In the present case no written notification has been given.
- 2. Contrary to the allegation that the methodology of testing for darbepoetin is experimental and not legally nor scientifically accepted, evidence was given as to the methodology and reliability of the combined blood and urine test. The existing test for EPO whether natural or recombinant can be used without modification to detect darbepoetin. On the basis of the existing evidence, the CAS considers that the methodology of testing for erythropoietin and darbepoetin is scientifically sound, and that the results produced by the tests are reliable.

On the 21st February 2002, during the Olympic Winter Games 2002, L., a cross country skier who represents Russia in International Competition, was due to participate in the 4x5 kilometre women's relay cross-country skiing race. She was selected, at random, to undergo a drug test before the race. Accordingly, about one hour before the start of the race, the World Anti-Doping Agency ("WADA") representatives took a sample of her blood. WADA was responsible, throughout the Olympic Winter Games, for the conduct of anti-doping tests on behalf of the IOC.

The analysis of L.'s blood sample indicated that there was a level of haemoglobin in excess of the level of 16 g/dl, which was the cut-off point for competition prescribed by the IOC Blood Testing Statement.

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<sup>\*</sup> NB: An appeal has been filed against this award before the Swiss Federal Tribunal (réf. 4P.267, 268, 269 & 270/2002); it has been dismissed on 27 May 2003. Cf. ATF 129 III 425.

In accordance with the Medical Guide, L. was asked to provide a second blood sample. Again, the haemoglobin level was in excess of the cut-of point for competition. Accordingly, L. was not permitted to start the race. The Russian team thereupon decided, in protest, not to take part in the

L. was then requested to provide a urine sample. That sample, together with the sample of blood, was taken to the IOC accredited laboratory in Salt Lake City.

On the Doping Control Form, which was completed at the time of the taking of the urine sample, L., stated that in the three days prior to the 21st February 2002 she had taken "Hameton spzei" (in fact, Kameton) and Vitamin B complex.

On the 21st February 2002 the samples were duly analysed at the IOC accredited laboratory in Salt Lake City, and on the 23rd February 2002 the acting Chairman of the IOC Medical Commission was informed of a positive finding on L.'s "A" urine sample. The analytical finding was of the presence of Darbepoetin (Aranesp = NESP). The Russian National Olympic Committee ("RNOC") was informed that Aranesp (darbepoetin) had been discovered in L.'s urine sample.

The acting Chairman of the IOC Medical Commission appointed an Inquiry Commission. The Inquiry Commission met at 11.00pm on the evening of the 23rd February 2002. Representatives of the RNOC attended. L. did not attend.

At the conclusion of the hearing the Inquiry Commission concluded that the evidence demonstrated that darbepoetin had been present in L.'s urine sample, and that darbepoetin was an analogue/mimetic of erythropoietin, which is a prohibited substance under OMAC.

The Inquiry Commission, therefore, decided that L. had committed a doping offence of using a substance contrary to Chapter II, Articles 2.1 and 2.2 and Appendix A Part I Paragraph E of OMAC. The Inquiry Commission referred the case to the IOC Disciplinary Commission, which, on the morning of the 24th February 2002, held a meeting to consider the matter. The same representatives of the RNOC who had attended the Inquiry Commission meeting were in attendance.

However, before the IOC Disciplinary Commission had concluded its consideration of L.'s case, L. competed in the women's 30 kilometre classical cross-country skiing race, which she won.

The Disciplinary Commission concluded that L. had committed a doping offence. On the 24th February 2002 the IOC Executive Board accepted the conclusions and recommendations of the Disciplinary Commission, and disqualified L. from the women's 30 kilometre classical cross-country skiing race, ordered the withdrawal of her medal and diploma and ordered her exclusion from the Olympic Winter Games 2002.

The IOC Executive Board also requested the FIS to modify the results of the race, and to consider any further action within its own competence.

On the 26th February 2002, at the request of the FIS and in the presence of representatives of RNOC, L.'s B sample was analysed. Again, this showed the presence of darbepoetin.

L. did not request a hearing, and did not make a written statement. At its meeting on the 3rd June 2002 the FIS Council suspended her for two years from the 21st February 2002.

The Inquiry Commission, the Disciplinary Commission and the IOC Executive Board considered the case against L. at the same time as it considered a similar case against another member of the Russian women's cross-country skiing team, D.

D. was also found by the IOC Disciplinary Commission to have taken a prohibited substance, darbepoetin, and was also excluded from the Olympic Winter Games 2002 by the IOC Executive Board. She is appealing against that decision. Subsequently, D. was also suspended for two years by the FIS Council. D. is also appealing to the CAS against her exclusion and suspension. Her appeals are being heard by this Panel (CAS 2002/A/371 [IOC] and CAS 2002/A/398 [FIS]).

The issue in this appeal can be shortly stated. L. contends that the methodology of testing for darbepoeitin is experimental, and is neither legally nor scientifically accepted. In particular, she contends that it is not permissible to use the method of testing for erythropoietin in order to test for darbepoetin. Furthermore, she contends that the test on the B sample was improperly carried out as the urine sample was poured from the sample bottle into a dirty, non-sterile container. There was, therefore, she submits, a danger of contamination.

The IOC disputes L.'s contentions. It submits that darbepoetin can be detected by the same test commonly used and recognised for the detection of erythropoietin. It refutes the suggestion that there was any danger of contamination in the test on the B sample. Furthermore, the IOC submits that, even if, contrary to its primary submission, the test on the B sample was in any way flawed, there was and could not be any such criticism of the test on the A sample. The IOC was prepared to rely on the A sample alone.

Substantially the same issues in relation to the methodology of testing for darbepoetin are raised in this case as are raised in L.'s appeal against the suspension ordered by the FIS in Case No. CAS 2002/A/397. However, this appeal will become redundant if L. does not succeed in the appeal against the FIS suspension because the FIS suspension was deemed to commence on the 8th December 2001. If that suspension is upheld, L. would have been ineligible to participate in the Olympic Winter Games.

At the commencement of the hearing, the Counsel for L., made an application that the entire Panel should recuse itself. The precise basis for the application was never made clear to the Panel, and, in at least one respect, the application was unique in the experience of the Panel members in that it included an application that the member of the Panel nominated by L. should recuse herself. The Counsel for the Appellant seemed to be concerned that members of the Panel had, or were believed to have, sat with each other, or with persons, such as Mr Stiffler, Counsel for FIS, who were themselves known to such persons.

The application was not made in accordance with the provisions of Rule R34 of the Code of Sportsrelated Arbitration. Rule R34 is in the following terms:

"An arbitrator may be challenged if the circumstances give rise to legitimate doubts over his independence. The challenge shall be brought **immediately** after the ground for the challenge has become known.

Challenges are in the exclusive power of the ICAS which may exercise such power through its Board in accordance with the Statutes which are part of this Code. The petition setting forth the facts giving rise to the challenge shall be lodged by a party. The ICAS or its Board shall rule on the challenge after the other parties, the challenged arbitrator and the other arbitrators have been invited to submit written comments. It shall give brief reasons for its decision." (emphasis added)

Notwithstanding this procedural error, the Panel decided to treat the application as one based on apparent bias rather than upon the actual bias of the members.

The Panel considered that the appropriate test as to whether or not apparent bias might exist was whether in all the circumstances relied upon a fair-minded and informed observer would be led to conclude that there was a real possibility, or a real danger, that the tribunal was biased. Applying that test, the Panel was quite satisfied that no fair-minded and informed observer would have been led to that conclusion. Indeed, each member of the Panel was of the opinion that insofar as the fairminded and informed observer would have understood the application, he or she would have had no doubt about the ability of the individual members of the Panel to apply his or her mind independently to the issues in the appeal. In these circumstances, each member of the Panel refused to resign.

It subsequently became clear that the application was probably not even put on the basis of apparent bias because, in his final submissions, the Counsel for the Appellant made it clear that the application was not made because L. thought that the Panel would not make its decision according to the evidence: she accepted that the Panel would base its decision only on the evidence that it had heard. That concession appeared to rule out both actual and apparent bias.

## LAW

- There is no issue between the parties as to the jurisdiction of the CAS. That jurisdiction is 1. founded on Article 74 of the Olympic Charter, which is in the following terms:
  - "Any dispute arising on the occasion of, or in connection with, the Olympic Games shall be submitted exclusively to the Court of Arbitration for Sport, in accordance with the Code of Sports-Related Arbitration."
- 2. Both erythropoieitin and darbepoetin are substances used in what is commonly known as "blood doping". They work by stimulating the production of red blood cells. Such increased production is capable of enhancing performance in endurance sports, such as cross-country

- skiing. However, both substances can damage the health of the taker by increasing the viscosity of the blood.
- There are two types of erythropoietin: erythropoietin which is naturally produced in the body, 3. and artificial, or recombinant, erythropoietin.
- 4. Darbepoetin is unlike natural erythropoieitin, but like recombinant erythropoietin, in that it is an artificial substance which is not naturally produced by the human body. Its presence in blood or urine can only be as a result of exogenous ingestion. By contrast, natural erythropoietin is only endogenously produced. The particular type of darbepoetin found in L.'s urine sample was Aranesp = NESP (Novel Erythropoeisis Stimulating Protein).
- 5. Aranesp is the trademark of Amgen Inc. ("Amgen") for darbepoetin alfa, which is a novel erythropoeisis stimulating protein produced by recombinant DNA technology. It is produced in Chinese hamster ovary cells, and stimulates red blood cell production by the same mechanism as recombinant human erythropoietin. Aranesp is a 165-amino acid protein, which contains 5 N-linked oligosaccharide chains: erythropoietin contains only 3 such chains. The additional chains increase the molecular weight of the glycoprotein by just under 25%. Aranesp is a sterile, clear, colourless, preservative-free aqueous solution for parenteral administration. It is available in single use, pre-filled syringes, but can be administered either subcutaneously or intravenously.
- 6. The particular medical use to which Aranesp has been put is the stimulation of erythropoiesis in anaemic patients who are suffering from chronic renal failure. The result of its use is the correction and maintenance of haemoglobin levels. In adults suffering from chronic renal failure the terminal half-life of Aranesp is approximately 21 hours following intravenous administration, and approximately 49 hours following subcutaneous administration.
- 7. The particular advantage of Aranesp in comparison with erythropoietin, whether natural or recombinant, is that because its half-life is much longer than either natural or recombinant erythropoietin, it has to be administered less frequently than either of them.
- 8. Although darbepoetin is not specifically listed as a prohibited substance in the Olympic Movement Anti-Doping Code ("OMAC"), it was accepted on behalf of L. at the hearings in Salt Lake City, and by Professor Durmanov at the hearing before the Panel, that it is an analogue or mimetic of erythropoietin. Thus, in accordance with Appendix A Part I Paragraph E of OMAC, its use is permitted only to treat insulin-dependent diabetes and, even then, only if written notification has been given prior to the particular competition by an endocrinologist or the team physician. Furthermore, OMAC provides that:
  - "The presence of an abnormal concentration of an endogenous hormone or its diagnostic marker(s)in the urine of a competitor constitutes doping unless it has been conclusively documented to be solely due to a physiological or pathological condition."
- 9. For the sake of completeness, the Panel would wish to record that (a) no written notification was given on L.'s behalf that she was using Aranesp=NESP to treat insulin dependent

diabetes, and no suggestion to that effect was made during the hearing and (b) if it had been necessary to decide the issue, it would have held that darbepoetin was an analogue or mimetic of erythropoietin, and, therefore, a prohibited substance.

- 10. For some time, and certainly throughout 2001, and at the Olympic Winter Games 2002, testing for erythropoietin involved the taking of an initial blood sample. The blood sample was analysed for haemoglobin and % reticulocytes. If the haemoglobin level exceeded 16 g/dl for women and 17.5 g/dl for men, a urine test for erythropoietin had to be taken. If the haemoglobin level was less than 16 g/dl for women and 17.5 g/dl for men, but the % reticulocytes exceeded 2, again a urine test for erythropoietin had to be taken.
- 11. On the 7th November 2001 the IOC issued a Press Release, which was sent to all International Federations, including the FIS, in which it was announced that, at a meeting arranged by the IOC Medical Commission, a panel of scientific experts had reviewed the criteria for detecting the presence of recombinant, or artificial, erythropoietin, and had reaffirmed a combined erythropoietin blood and urine test, and refined testing procedures. It was noted that the ability to detect the use of recombinant erythropoietin had improved as a result of the experience gained since the last meeting of experts in July 2000, prior to the Olympic Summer Games 2000 in Sydney.
- 12. The panel of experts concluded that, in order to recommend and support a finding of a positive doping result due to the presence of recombinant erythropoieitin in the body, the proper detection method was a combined erythropoietin blood and urine test in which both the blood sample and the urine sample had to return abnormal results. It was announced that this method of testing would be applied during the Olympic Winter Games 2002.
- 13. By letter dated the 18th January 2002 the IOC Medical Director, Dr Patrick Schamasch, informed a number of interested parties, including the FIS, of the arrangements for erythropoietin testing at the Olympic Winter Games 2002. In that letter, Dr Schamasch confirmed the levels described above as the relevant levels for haemoglobin and % reticulocytes. Under the heading "Clarifications Regarding the Operational Plan For Blood Testing at the 2002 Salt Lake City Olympic Winter Games" it was stated:

"C. With regard to the blood parameters that will be measured on the venue and in the IOC Laboratory:

The IOC and WADA have recognized that the analysis of blood in the field for the two parameters, hemoglobin and % reticulocytes, is sufficient to support the finding of EPO in urine using the French urine method....".

The method to which reference was there made is the method developed by Professor Françoise Lasne and others.

14. The blood test described above is the trigger which leads to the requirement for an athlete to provide a urine sample so that it can be discovered whether the athlete has a prohibited substance in his or her body.

- The presence of any form of erythropoietin, recombinant erythropoietin or darbepoetin is 15. absolutely prohibited. There is no question of there being a permitted level of either substance. Its presence is only permissible in the circumstances described in Paragraph 5.6 above. In this sense, erythropoietin, recombinant erythropoietin and darbepoetin are different in kind from those substances in which there is a permitted level and a prohibited level.
- 16. The same combined test was used to discover if darbepoetin had been used by an athlete.
- 17. There is no dispute that the burden of proving that L. is in breach of the provisions of OMAC is on the IOC. Thus, the IOC must prove that (a) the sample was properly taken; (b) there was a complete chain of custody of the sample from the Doping Control Centre to the laboratory; and (c) the test used was a reliable test for the discovery of the presence of a prohibited substance.
- Once the sample is at the laboratory, there is a presumption that the testing and custodial 18. procedures have been conducted in accordance with prevailing and acceptable standards of scientific practice. The presumption can be rebutted by convincing evidence to the contrary, but there is no evidential burden on the laboratory to show that it conducted the procedures other than in accordance with its customary practices: see OMAC, Chapter III, Article 2.
- Thus, L. has the burden of proving either that the analysis of the sample was not conducted in accordance with the laboratory's customary practices or that the laboratory's customary practices were not in accordance with prevailing standards of scientific practice and were, therefore, unacceptable.
- In these appeals the sanction imposed by the IOC was, in each case, disqualification. CAS 20. jurisprudence recognises that when disqualification is the sanction, a breach of the relevant anti-doping rule is of strict liability. By contrast, where the sanction to be imposed includes suspension, the subjective circumstances surrounding the athlete's use of the prohibited substance may be taken into account.
- So far as the standard of proof is concerned, the Panel will apply the normal CAS standard that disputed facts have to be "established to the comfortable satisfaction of the court bearing in mind the seriousness of the allegation": see CAS OG/96/004 K & G v/ IOC; CAS 98/208 N v/ FINA; Swiss Federal Tribunal Judgment 31st March 1999.
- There does not appear to be any dispute about either the taking of the sample or the chain of custody of the sample from the Doping Control Centre to the laboratory. However, there is alleged to have been an irregularity in the testing of the B sample in each case. As has been stated above, the burden of proving an irregularity in laboratory procedure rests on L. The consequence of such an irregularity, if proved, will be considered later in the Award. The real issue of dispute, however, was as to the reliability of the combined blood and urine test used.

- 23. The Panel heard evidence from a number of witnesses. However, L. did not give evidence. Her failure to do so led to strong comment from the IOC, whose Counsel described her as a "disgrace" and "the most heavily doped athlete in Olympic history".
- Professor Don Catlin, who is a Professor of Molecular and Medical Pharmacology and the director of the Paul Ziffren Olympic Analytical Laboratory at the University of California in Los Angeles and Dr Steve Elliott, who has a PhD in Molecular Biology and Biochemistry, and is employed by Amgen, the manufacturers of Aranesp, gave evidence on behalf of the IOC.
- 25. Professor Catlin has been involved for many years in the testing of body fluids and in research on the detection of doping agents. He ran the IOC laboratory at Salt Lake City.
- 26. Amgen has been responsible for the invention and development both of the first recombinant human erythropoietin product and, through Dr Elliott, of darbepoetin alfa. Darbepoetin alfa is sold throughout the world under the brand name Aranesp, and is an analogue of recombinant human erythropoietin.
- 27. Both Professor Catlin and Dr Elliott gave evidence as to the methodology and reliability of the combined blood and urine test. The test itself is described elsewhere in this Award. It is sufficient for present purposes simply to state that both of them expressed the opinion that the test was reliable, and that, because of the particular molecular structure of darbepoetin, it was particularly reliable for detecting the presence of that substance. Darbepoetin was chemically and pharmacologically similar to erythropoietin, and the effects of its use were the same.
- In his written statement Professor Durmanov put forward no positive evidence in relation to the methodology of testing for erythropoietin or darbepoetin. Instead he posed a series of questions. The Panel is bound to say that this was not the most helpful way for an expert to give evidence. It would have been more helpful if Professor Durmanov had assisted the Panel by stating in his statement whether, in his opinion, the methodology was reliable and whether accurate and reliable results were produced by the testing.
- 29. When he came to give evidence at the hearing, Professor Durmanov contended that the methodology had not been "validated", by which he meant that it had not been sufficiently published and discussed in medical circles. He was unwilling to accept that meetings of those involved in the carrying out of anti-doping procedures, and their approval of the methodology of such procedures, was sufficient validation. He said that it was not enough for the test simply to the "valid" that is to be a test which does not produce false positives. Until it had been validated, it could not be used to determine whether or not erythropoietin or darbepoetin had been used.
- In the event, the Panel has no hesitation in accepting the evidence of Professor Catlin and Dr Elliott in preference to that of Professor Durmanov, whose evidence seemed to be substantially influenced by a frustration at the lack of funds available for anti-doping research in Russia and a perceived inequality of treatment of Russian doctors and athletes.

- 31. The consequence of accepting the evidence of Professor Catlin and Dr Elliott is that the Panel finds that:
  - (a) the method of testing for darbepoetin is reliable;
  - (b) the test results in L.'s case proved that she had a prohibited substance, darbepoetin, in her blood when she competed in, and won, the women's 30 kilometre classical cross-country skiing race; and
  - (c) L. was in breach of the provisions of OMAC and of the Medical Guide.

As has been stated above, L. did not give evidence and there has been no explanation from her as to how that prohibited substance came to be in her blood. In the light of that failure to explain, the Panel concludes that the prohibited substance was in L.'s blood as a result of intentional exogenous ingestion by her.

- 32. The Panel, therefore, concludes that the decision by the IOC Executive Board on the 24th February 2002 that L. should be disqualified from the women's 30 kilometre classical cross-country skiing race; her medal and diploma should be withdrawn; and she should be excluded from the Olympic Winter Games, was correct.
- 33. However, in view of the importance of this case, and of the associated cases, in relation to the fight against doping, and of the fact that these cases require a decision on the methodology and reliability of testing for recombinant erythropoietin (and darbepoetin), the Panel will make specific findings on the evidence as to the methodology and reliability of the tests carried out.
- 34. While darbepoetin is structurally distinct from recombinant human erythropoietin, it increases haemoglobin concentrations in human blood by the same mechanism as recombinant human erythropoeitin. "Like endogenous and recombinant erythropoietin, darbepoetin acts on erythroid progenitor cells to stimulate red blood cell productions": The Medical Letter (2001), Volume 43, page 109-110. However, the structural characteristics of darbepoetin give it an increased biological activity in consequence of its longer serum half-life.
- 35. Endogenous erythropoietin, recombinant human erythropoietin and darbepoetin produce their physiological action by binding to erythropoietin receptors. The result of that action is to produce physiological effects. Each of the substances produces the same physiological effects.
- 36. Red blood cells transport oxygen to tissues in the human body and, as physical exercise is limited, to some extent, by the amount of oxygen that is delivered to muscle tissue, some athletes seek to enhance their performance by increasing the production of red blood cells. Erythropoietic products, such as erythropoietin, recombinant human erythropoietin and darbepoetin, can produce the desired results.
- 37. Testing for erythropoietin and its analogues at the Olympic Winter Games 2002 involved an indirect blood test and a direct urine test.

- The indirect blood test was developed by Australian scientists prior to the Olympic Summer Games 2000. It was intended as a screen test to limit the number of samples from athletes who would then have to undergo the direct urine test. The indirect blood test produced what was known as the "Sydney on-score", which was an index of erythropoietic activity based on five separate blood parameters. Those parameters are the measurements of reticulocytes, macrocytes, haematocrit, the concentration of transferrin receptors in serum and the concentration of erythropoietic in serum.
- The athlete's blood sample is tested for these parameters, and the results are entered into a 39. mathematical formula to give an "on-score". If the "on-score" is above a certain threshold, an abnormally high level of erythropoietic activity is indicated. The athlete is then required to submit a urine sample for the direct erythropoietin test.
- 40. Darbepoetin has the same effects on the blood parameters as does recombinant human erythropoietin. Thus, a high "on-score" reflects the use of some substance that elevates the erythropoietic activity.
- The "on-score" recorded for L. was 3.37, which was the highest value observed for any 41. athlete, male or female, at the Olympic Winter Games 2002. The threshold "on-score" level for female athletes was 2.35, and the range of values at the Olympic Winter Games 2002 was between 2.16 and 3.37.
- 42. The direct urine test involves four procedures: sample preparation, isoelectric focusing, immuno-blotting and visualisation.
- 43. Two steps are involved in sample preparation. The first step involves rendering inactive enzymes which could destroy the erythropoietin or darbepoetin before the isoelectric focusing stage. The second step involves the removal of materials in the urine that are detrimental to the analysis.
- 44. The proteins, such as erythropoietin, recombinant human erythropoietin and darbepoetin are concentrated by the addition of protease inhibitors to render the enzymes inactive, and then special filters are applied that removed molecules with a low molecular weight. Darbepoetin has a high molecular weight. In order to remove those molecules, the urine is placed in a cup, which is placed in a centrifuge. As the cup spins, the low molecular weight material passes through the filter, leaving what is called "the retentate".
- 45. This step is repeated. If erythropoietin, recombinant human erythropoietin or darbepoetin is present, it will be found in the retentate, which is left after the second filtration. The retentate is liquid.
- Part of the retentate is used to calculate the concentration of darbepoetin by means of an immunoassay. This gives an estimate of the amount of darbepoetin in the urine sample. The estimated amount is used to adjust the concentration of darbepoetin in the retentate to a uniform value, so that there is no excessive concentration in the retentate. If this step were

- not taken, it would make the interpretation of the electropherograms, which are produced in the next procedure, difficult to interpret.
- Once the adjustment has been made to the concentration of darbepoetin in the retentate, a 47. portion of the urine is "spotted" onto a gel. The gel is about 25 centimetres in length by 12 centimetres in width and about 1 millimetre thick. The gel serves as the "platform" for the electrophoresis. Electrodes are attached to the gel, and connected to the electrophoresis instrument. One of the electrodes is the anode, and the other is the cathode. A current is applied to the gel for half an hour in order to establish the pH gradient of the molecules in the gel.
- After the pH gradient has been established, the samples and standards that are to be 48. electrophoresed are "spotted" onto the gel by adding a small volume of each sample to a piece of filter paper that has been placed on the gel. The pieces of filter paper are placed 1 centimetre apart, close to one edge of the gel, which can accommodate about 24 pieces of filter paper. In this way, the surface of the gel is divided into what are described as 24 lanes.
- 49. Each sample or standard is "spotted" on one lane. Typically, one or two different standards are used, of which there are one or more control samples, whose content is known, and a number of samples, whose content is unknown. The control samples will usually be of pure recombinant human erythropoietin, or pure darbepoetin, or a mixture of the two, and will be obtained from a person to whom pure recombinant human erythropoietin or pure darbepoetin has been administered.
- The current is turned on for 2 1/2 hours, or such period as gives all the molecules sufficient 50. time to migrate or move to their isoelectric point. Once they have reached that point, they remain stationary. Interpretation of the electropherogram can then take place.
- Darbepoetin has four bands. These are known as isoforms, which is a sub-set of the 51. darbepoetin molecules with a defined charge. The molecules of darbepoetin migrate to the anode side of the electropherogram, because they have a preponderance of negative charges, while the molecules of recombinant human erythropoietin migrate to the cathode side, because they have fewer negative charges. Thus, recombinant human erythropoietin and darbepoetin will be separated by several centimetres of physical space on the electropherogram. Natural erythropoietin will appear somewhere between recombinant erythropoietin and darbepoetin.
- 52. The next step is to remove the bands from the gel, and to mark them so that their location can be observed with the naked eye. This step is accomplished by "blotting", which is a procedure for transferring proteins from one surface to another.
- Two "blotting" procedures are used. The first procedure transfers the proteins from the gel to a membrane. In order to achieve this transfer, the gel is removed from the electrophoresis plate and washed with a buffer. It is then placed between two stacks of paper, which have been soaked in a special blotting buffer. The two stacks of paper, together with the gel, are

placed between two plates through which an electric current is applied for 30 minutes. The membrane which is produced by this procedure is a mirror image of the material that was on the gel.

- The membrane is then incubated in a solution of antibodies against erythropoietic proteins. The antibodies are produced in mice, which have been immunised with an erythropoietin-like material.
- 55. The antibodies are removed from the membrane, and transferred to a second membrane. The molecules of the erythropoietin and darbepoetin remain on the first membrane. The second membrane is then incubated in a solution which contains a second antibody, which specifically binds to the first antibody. The second antibodies mark the location of the recombinant human erythropoietin and darbepoetin.
- Finally, a marker protein, which binds to the second antibody is applied, and a light-emitting substance is added, which emits light when it comes into contact with the marker protein. The emitted light is then photographed by a special digital camera. The image is used to evaluate the results.
- The UCLA Olympic Analytical Laboratory has received ISO certification for the 57. erythropoietin test. The certification establishes that the laboratory is capable of performing the test, and that the test performs in the manner expected. The temporary laboratory set out by the UCLA Olympic Analytical Laboratory in Salt Lake City for the Olympic Winter Games 2002 was also ISO certified.
- Professor Catlin told the Panel that there was no difficulty in detecting darbepoetin by using the existing test for recombinant human erythropoietin, and that the test needed no modification. This is because the location of darbepoetin on the gel, and the pattern of its bands, is completely distinctive from the location and pattern is by erythropoietin.
- 59. Most importantly, Professor Catlin said, and the Panel accepts, that the test was designed to eliminate the possibility of false positives, that is that a positive result would be shown for an athlete who had not exogenously ingested either recombinant erythropoietin or darbepoetin.
- 60. Furthermore, since the Olympic Winter Games 2002, Professor Catlin has performed two further studies on the pharmacology and detection time of darbepoetin. Those studies have confirmed the methodology and reliability of the tests for darbepoetin.
- 61. In the light of the evidence, the Panel has no hesitation in finding that the methodology of testing for erythropoietin and darbepoetin is scientifically sound, and that the results produced by the tests are reliable.
- When the B sample was being tested, the head of the Russian Mission, Mr Victor Mamatov, 62. noted that "the pouring of urine from sealed bottle of urine was poured into unsterile tubes, which were located on the shelf not in any visible packaging". Thus, it was contended that the

- B sample was, or may have been, contaminated, and that the result obtained from testing it was unreliable.
- Although his name had been on the list of witnesses, Mr Mamatov did not make a statement, 63. and did not give evidence at the hearing.
- 64. Professor Catlin told the Panel that it was not necessary to use sterile tubes, and that there never had been any such necessity.
- 65. The Panel has no hesitation in accepting Professor Catlin's evidence on this issue. It is significant that Professor Durmanov was not asked, and expressed no view, about the testing of the B sample or the use of "unsterile tubes".
- In these circumstances, the Panel takes the view that there is no substance in the criticism noted by Mr Mamatov at the time that the B sample was tested.
- 67. For all the above reasons, L.'s appeal must be dismissed.

## The Court of Arbitration for Sport hereby rules that:

- 1. The appeal filed by L. on 13th March 2002 is dismissed.
- 2. The decision of the IOC Executive Board of 24th February 2002 is confirmed.
- 3. (...).