Expert Opinion

Responsible for the Content

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This document represents my response to the letter of instruction for expertise that I received from the IAAF regarding the analysis of sample 10E003 4433, reported as an adverse analytical finding for CERA by the WADA-accredited laboratory in Rome, Italy.

The IAAF's questions are presented in *italics* below and my answers are in normal type.

1. *Please describe the analytical method currently used by WADA-accredited laboratories for the detection of recombinant erythropoietins and analogues in doping control samples, including CERA.*

   According to the TD2009EPO there is currently one method for the detection and confirmation of recombinant forms of erythropoietin mandatory in urinary doping control samples and this is called the Isoelectric Focusing (IEF) test.

   The IEF method for the detection of rEPO and analogues in doping control samples as briefly described in the TD2009EPO is based on ultrafiltration, isoelectric focusing, double blotting and chemiluminescence detection. This method was developed and published basically by Dr. F. Lasne from the French doping control laboratory.

   The method uses at least three independent principles to gain specificity:

   - IEF separation of EPO isoforms according to their isoelectric properties
   - a monoclonal antibody to specifically locate EPO isoforms on the membrane
   - a second blotting step as a key improvement to significantly reduce possible interference of urinary proteins with the non-specific second antibody

   The method is accepted by WADA since many years as the standard method to detect the misuse of rEPO and analogues in sports, including CERA.

   Additional evidence: If the IEF results in any case show a profile that is not consistent with a typical endogenous profile but do not allow a final conclusion, the Technical Document allows as additional evidence methods like SAR PAGE and SDS PAGE to help confirm the nature of the finding.

   Unlike IEF-PAGE, the SDS PAGE method uses molecular weight instead of isoelectric properties. However, SDS-PAGE has been shown to be less sensitive for CERA than for the other epoetins, because of interference of the SDS – containing PEG group of the CERA molecule with the primary

antibody used for the Western blot (clone AE7A5)[1]. Consequently, this method is not recommended for helping to confirm CERA in doping control samples. Our laboratory recommends instead the use of Sarcosyl-PAGE which was introduced to solve the problem of the reduced sensitivity with SDS-PAGE. SAR-PAGE, similar to SDS, is an anionic detergent but, unlike SDS, hardly interacts with the PEG group of CERA and only with the protein chain. As a result, CERA migrates as a sharp band in SAR-PAGE and is detected with the same sensitivity as other epoetins by the primary antibody.

2. *Please comment on the general criticisms of the test method that have been cited by Mr Tysse (see articles at Appendix 7 of Mr Tysse's Appeal Brief).*

The IEF method is extensively published by the anti-doping community and the publications have undergone peer-reviews. Criticism of the method mainly focuses on the specificity of the antibody used. In this respect, it has to be stated that the monoclonal antibody is not the sole source of specificity of the method. The electrophoretic behavior as well as the double-blotting procedure adds important contributions to the specificity of the overall method.

The articles by Khan[2], Beullens et al.[3], and Franke et al.[4] caused at least as many counter-articles to be written due to the content contained in them. These publications e.g. by Khan et al.[5,2] contain errors e.g. all of the 4 proteins which are claimed by Khan et al.[5] to be bound non-specifically by the clone AE7A5 antibody are in fact NOT bound by clone AE7A5 in combination with the 1D carrier ampholyte (CA) IEF-PAGE used in anti-doping control. This has been shown by several labs including our lab[6]. Obviously, nearly no one who cites Khan's publication regarding the non-specificity of the antibody has ever tested the binding behaviour in this context.

In fact, Khan et al. drew the fatal conclusion that, whatever happened on their 2D-PAGE method, was also true for the CA-IEF-method. Khan has never shown this (and later admitted this fact in a published article[7])

In conclusion: the expertise behind these publications is questionable with respect to EPO anti-doping testing and in no way undermines the validity of the IEF test method used.

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[1] C. Reichel, F. Abzieher, T. Geisendorfer. SARCOSYLPAGE: a new method for the detection of Mircera- and EPOdoping. in blood. Drug Test Anal, 1 (2009) 494–504.

[2] A. Khan, MS. Baker MS. Non-specific binding of monoclonal human erythropoietin antibody AE7A5 to Escherichia coli and Saccharomyces cerevisiae proteins. Clin Chim Acta 379 (2007) 173–175.

[3] M. Beullens, JR. Delanghe, M. Bollen. False-positive detection of recombinant human erythropoietin in urine following strenuous physical exercise. Blood 107 (2006) 4711–4713.

[4] WW. Franke, H. Heid. Pitfalls, errors and risks of false positive results in urinary EPO drug tests. Clin Chim Acta 373 (2006) 189–190.

[5] A. Khan, J. Grinyer, ST. Truong, EJ. Breen, NH Packer. New urinary EPO drug testing method using two-dimensional gel electrophoresis. Clin Chim Acta 358 (2005) 119–130.

[6] C. Reichel. Recent developments in doping testing for erythropoietin. Anal Bioanal Chem. (2011) [Epub ahead of print]

[7] A. Khan, N. Packer. Reply by the authors to "New urinary EPO drug testing method using two-dimensional gel electrophoresis". Clinica Chimica Acta 373 (2006) 188.

3. *Please explain the GasEPO software that is currently used to analyse images obtained in EPO analysis and comment on the criticism of this software by Mr Tysse's experts (section 5.1 of the Appeal Brief). Is the GasEPO software routinely used by WADA-accredited laboratories as a reliable interpretive tool in the conduct of EPO analysis?*

GASepo is an image evaluation software specifically designed by colleagues of the Research Center Seibersdorf with guidance by staff members of the Doping Control Laboratory to evaluate gel images for EPO testing methods. Knowledge from experienced colleagues from 10 different WADA accredited laboratories contributed to the first release of this software.

The software development was supported by two WADA grants. The algorithms used by the software for image analysis are published in peer-reviewed journals[8,9]. The software was validated by means of a phantom image demonstrating that no alteration of the raw image data occurs. The validation process included a cross-check with commercially available image processing software.

The software is now used by nearly all WADA-accredited laboratories which have the EPO detection method in place.

Finally, it is important to say that the software does not substitute knowledge, training and experience in the various EPO detection methods. It is regarded as a tool to visualize the raw data in support of the decisions of experienced specialists.

4. *Further to the Panel's order by letter dated 3 June 2011, please:*

(i) Provide a definition of "Band" according to regulations and laboratory practice;

(ii) Provide a definition of "corresponding" according to regulations and laboratory practice.

Generally speaking, a "band" is an area of signals which belong to the same origin e.g. in the case of IEF, a band means an area of aggregated EPO isoforms with similar isoelectric properties. These bands do not have to be completely separated.

In the case of CERA, these areas of aggregated EPO isoforms are comparatively close to each other as compared to other forms of rEPO. TD2009EPO requires at least 4 consecutive bands corresponding with the CERA reference substance.

The term "corresponding" in section 3.2.4 of TD2009EPO means that the 4 consecutive bands must be in the same general area as the CERA reference substance. It is important to note that CERA, due to the closer vicinity of its bands and their location on the gel, issues a very characteristic pattern that is notably different to the pattern normally found for endogenous origin. For this reason, TD2009EPO deliberately does not attribute numbers or letters for the corresponding assignment of the CERA bands to the reference standard like in the case of other epoetins and the intensity distribution is not regarded as necessary to be defined like in the case of e.g. epoetin alpha or beta. It is sufficient that the CERA bands are in the same area as the reference standard.

In this respect, it also has to be mentioned that the comparison of the location and intensity of the bands in the case of CERA in urine samples has to reflect the fact that the bands in the athlete's lane derive from CERA which has passed through the athlete's body, where it is the target of

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[8] I.Bajla, I.Holländer, G.Gmeiner, Ch.Reichel. Quantitative Analysis of Images in Erythropoietin Doping Control. Medical and Biological Engineering and Computing, 43, (2005) pages 403-409.

[9] I.Bajla, I.Holländer, M.Minichmayr, G.Gmeiner, Ch.Reichel. GASepo - a Software Solution for Quantitative Analysis of Digital Images in Epo Doping Control. Computer Methods and Programs in Biomedicine (2005), Vol. 80. Pages 246-270.

metabolism and slight structural changes; whereas the bands in the positive control sample as well as in the CERA standard lanes derive from a CERA standard preparation, which has not passed through any body. Whilst still in the same area as the CERA reference substance, the band intensities and band positions of the athlete's sample may thus be expected to differ slightly from the reference.

The following figures show the regions (indicated as yellow transparent bar), in which the bands of CERA, corresponding to the reference standards on the same gel image, in the urine samples of the athlete are to be expected. The lane containing the athlete's sample is indicated by a red arrow.

Figure 1 – Confirmation gel of the A-sample confirmation; the relevant region, where CERA bands are expected to be located, is indicated in yellow. Red arrow: lane containing the athlete's sample.

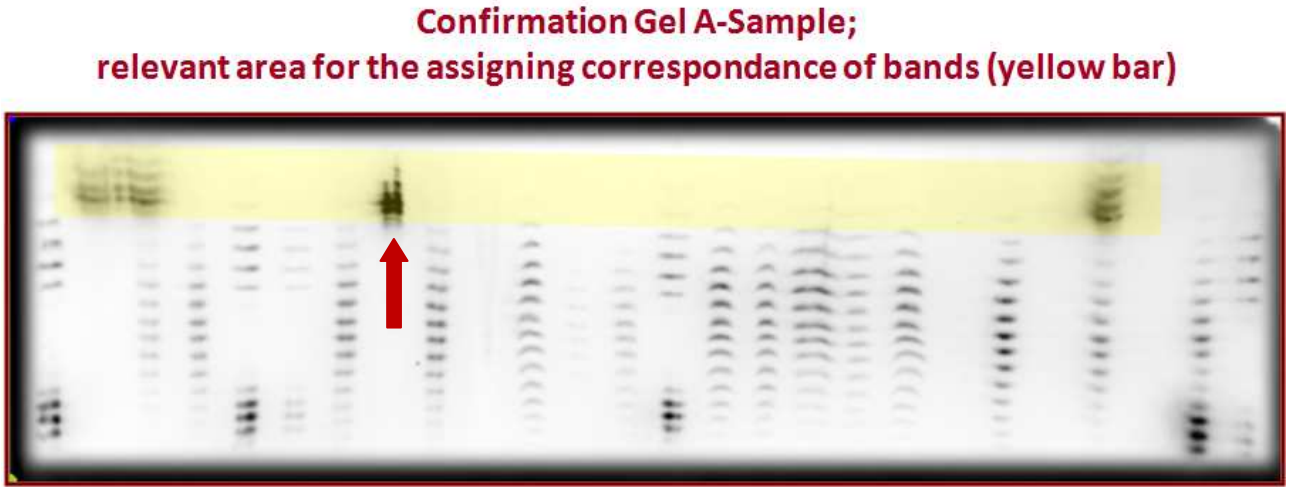
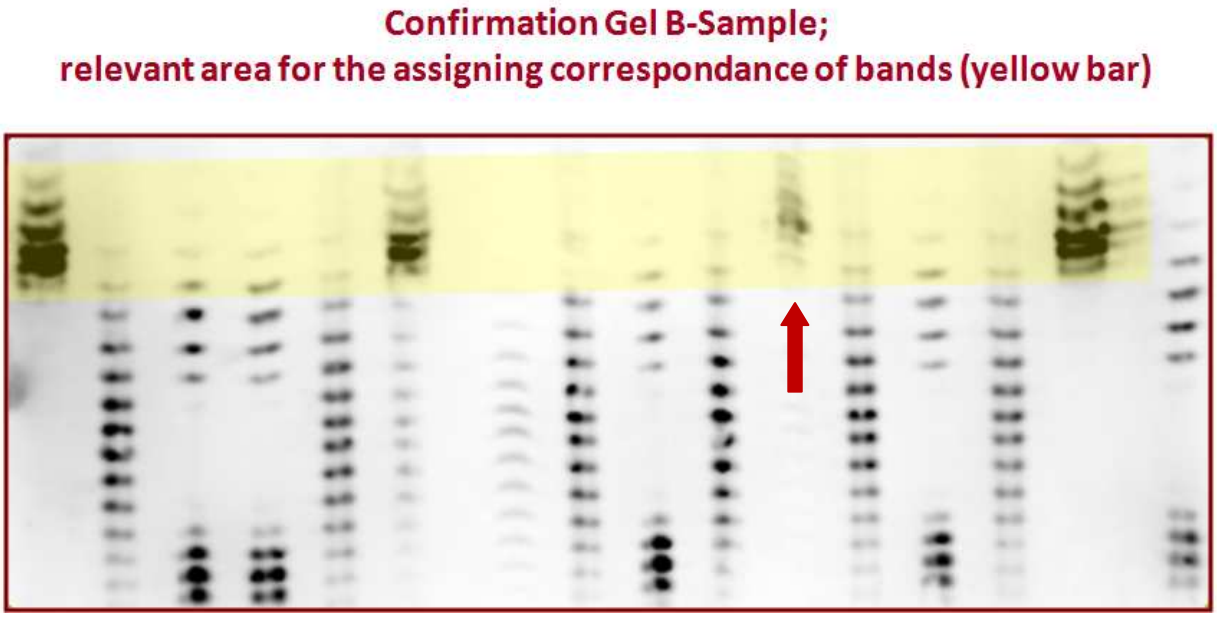


Figure 2 – Confirmation gel of the B-sample confirmation; the relevant region, where CERA bands are expected to be located, is indicated in yellow. Red arrow: lane containing the athlete's sample.



As clearly visible in the figures above, at least 4 bands of the CERA pattern in the athlete's sample are located in the region assigned to be the relevant area, where CERA bands are expected to be located.

5. *Please explain what is required from a laboratory director in providing a second opinion in respect of an adverse analytical finding for rEPO in accordance with WADA Technical Document TD2009EPO. In particular, is the laboratory director required for such purpose to conduct a completely new analysis of the sample in the director's own laboratory (see section 9.3 of the Appeal Brief)?*

A second opinion of an author of the TD2009EPO is mandatory before issuing an AAF for rEPO.

The author of the second opinion receives a set of data from the lab who has requested the second opinion. It is the responsibility of the author of the second opinion to get all the information needed to issue a second opinion. The sample is not re-analyzed.

The second opinion is provided according to the experience of the author. The interpretation of the analyzing lab and the opinion (second reading) of the author have to come to the same conclusion.

No particular form to provide the second opinion is defined. The author of the TD2009EPO providing a second opinion is therefore free in issuing the opinion in whatever form deemed to be appropriate.

6. Does the analysis conducted by the Rome Laboratory on sample 10E003 4433 disclose the presence of CERA in accordance with the International Standard for Laboratories and WADA's Technical Document TD2009EPO?

Yes, according to my review of the data submitted and the application of the set of criteria of the TD2009EPO relevant for the confirmation of the presence of CERA in urine, a conclusion that the sample contains CERA is justified.

The data submitted for review shows profiles in the basic region of the lane which significantly deviate from the profiles of endogenous origin normally found in human urine samples (see images in Figure 3). The location of the bands is in the region where the bands of the standard substance CERA appear, as demonstrated by the respective standard lanes. (Note that the laboratory decided to reject the first screening result and the first confirmation result from the B-sample analysis. Due to the fact that these results have to be nullified according to section 5.2.4.3.2.8 of the ISL, the evaluation of the data according to the TD2009EPO does not include these analyses).

For the three accepted determinations, there are no spots, smears or areas of excessive background significantly interfering with the bands visible on each lane (see Figure 4). The A-sample confirmation shows a small area of absent signal at the more basic band(s) but this does not invalidate the lane due to the fact that the bands are clearly visible. No quantification or ratio determination is necessary for the identification of CERA according to the TD2009EPO. A qualitative identification of four bands is sufficient to satisfy the TD2009EPO in this respect.

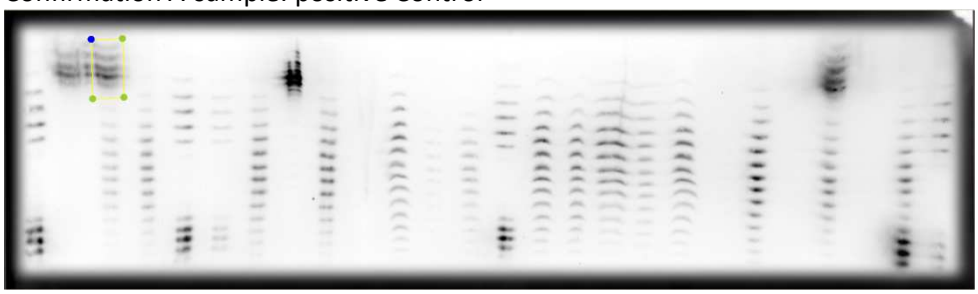
Comparison with a reference standard is also possible (see Figure 4, with the positive control samples taken as reference on the left and right side of the figure) and demonstrates that the bands appear in the same region and with a similar distribution as the CERA reference substance. It is important to note that the bands in the athlete's urine derive from excreted erythropoietin after body passage, whereas the bands in the reference lanes derive from a standard substance, which has not passed the body and excreted via the kidney. In addition IEF – gels for EPO analysis are not commercially available, but cast by hand before the analyses. Inhomogeneities cannot totally be excluded. A slight shifting in the band distribution, as well as in the position of the bands, as visible in the confirmation gels, is thus explainable.

On the repeated screening gel, as well as the confirmation gels, the sample lane shows in each case at least four bands as demonstrated on Figure 4 below. All images are screen copies from the GASepo software without manipulation of the raw data. The images provide a two dimensional as well as a three-dimensional (see Figure 5) impression of the raw data as provided by the Rome

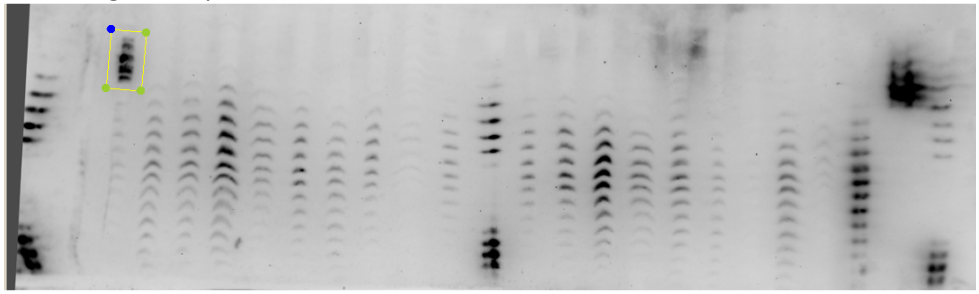
laboratory. The authenticity of the data can be confirmed by comparison of the images included in the full documentation packages.

Figure 3 – Regions of interests (yellow rectangles) relating to the images in Figure 4

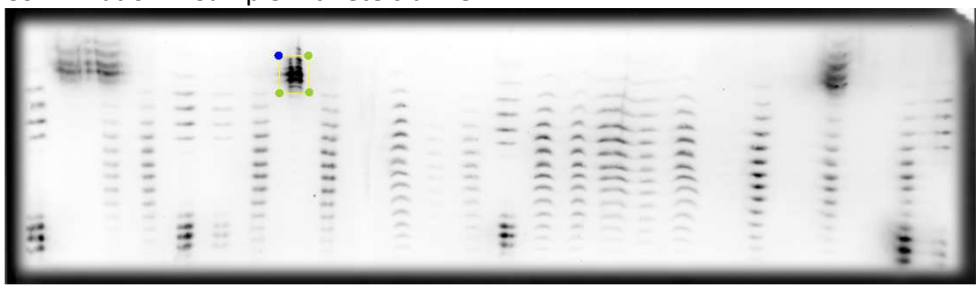
Confirmation A-sample: positive Control



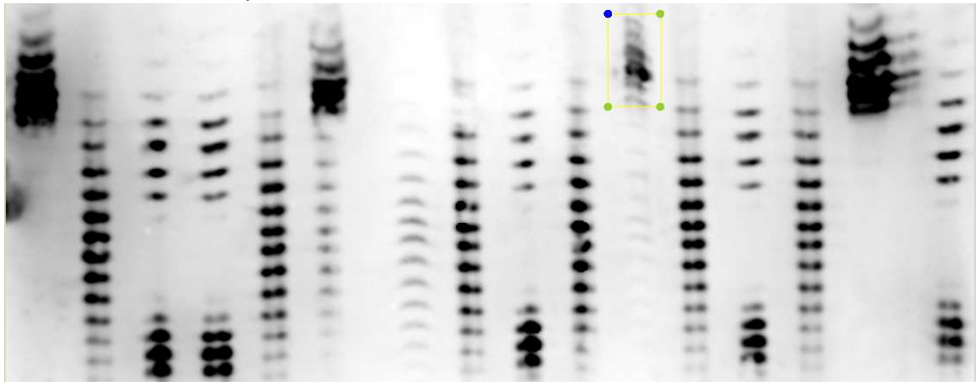
Screening A-Sample: Athlete's urine



Confirmation A-Sample: Athlete's urine



Confirmation B-Sample: Athlete's urine



Confirmation B-sample: positive Control

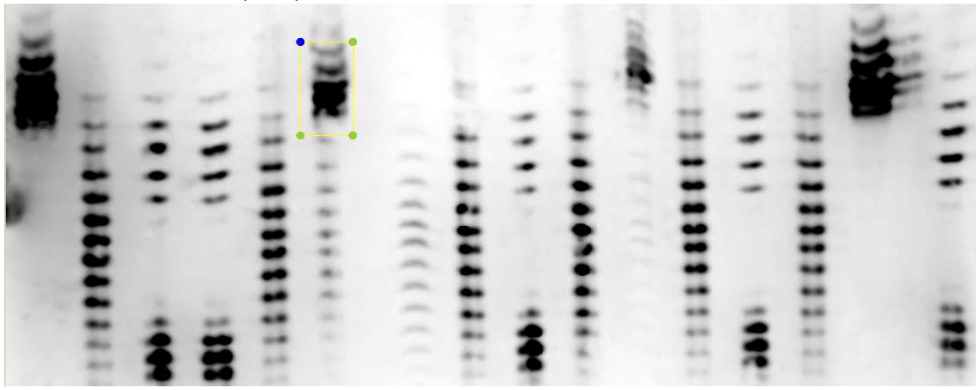
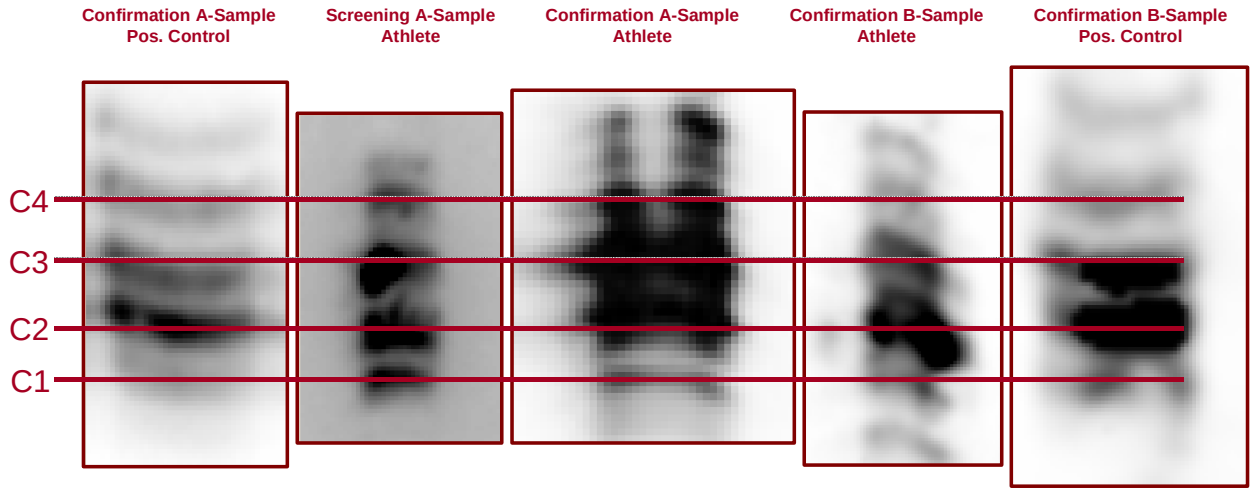


Figure 4 – Comparison of the band patterns of the athlete's samples accepted by the laboratory (second screening, A-sample confirmation, second B-sample confirmation) and the positive control urines on the same confirmation gels

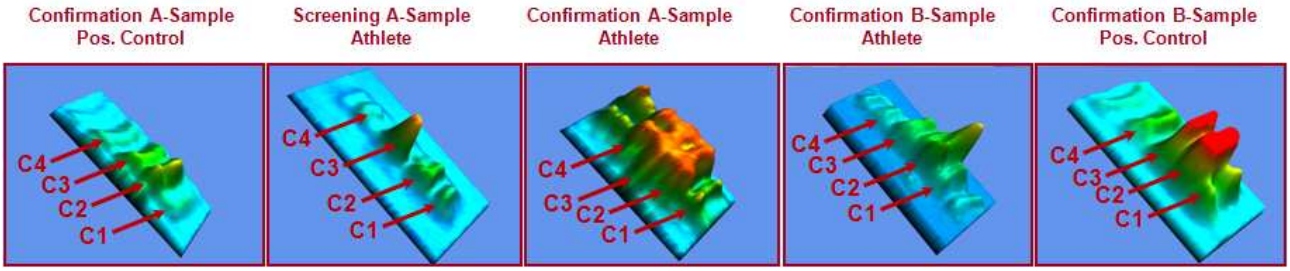


In the TD2009EPO, bands for CERA are not identified by numbers or letters, as in the case of rEPO or NESP. To be able to compare the four bands in each sample in Figure 4 above and in Figure 5 below, the band positions are indicated as C1 – C4 by the author of this document. C is meant to be a shortcut for CERA.

Due to the fact that the regions of interest of the three analyses of the athlete's sample derive from three different gels, the images are aligned in a way that the lowest band is in line for each of the images and the images are proportionately expanded. A distortion of the band distribution can be excluded.

The following Figures shows the same regions of interest of the gel images, as indicated in Figure 3 and demonstrated in Figure 4, as a three – dimensional plot. The bands in each of the windows are indicated according to Figure 4.

Figure 5 – three-dimensional view of the images in Figure 4; bands are indicated accordingly



From Figure 5, it can be seen that each analysis (screening as well as confirmations) shows at least four distinct bands, as required by the TD2009EPO.

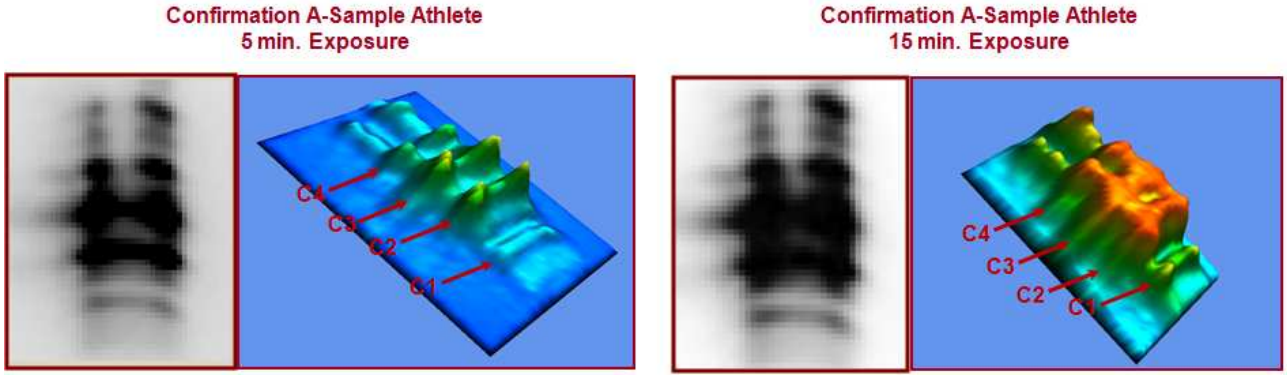
It can also be seen that the bands of the A-sample confirmation of the athlete's sample and the positive control of the B-sample confirmation are overexposed as indicated by the flat tops of the bands. Due to the fact that a quantitative evaluation of the lanes is not required for the identification of CERA, overexposure is not relevant as long as at least 4 bands can be identified.

Figure 6 further demonstrates clearly that 4 bands are present in the A-sample and B-sample confirmations. It compares a 5 minutes exposure time with the 15 minutes exposure time of the region of interest of the athlete's sample of the same gel image.

Exposure in this respect means that the second membrane was placed in the chemiluminescence camera after incubation with a chemiluminescence reagent and exposed to the light sensitive optics for a defined period of time. Longer exposure leads to a stronger signal, which may cause overexposure.

As mentioned above, the 15 minutes exposure shows at least 4 bands in the A-sample lane of the confirmation gel, which are overexposed indicated by a flat top (see Figure 6, right side). In comparison, the 5 minutes images show no sign of overexposure. The 4 bands are clearly visible in each case further confirming the acceptance as well as the identification criteria of the TD2009EPO to be fulfilled.

Figure 6 – Comparison of two exposure times of the relevant area of the gel image of the Athlete's confirmation sample; left: 5 Minutes exposure, right: 15 Minutes exposure



7. *What do the SDS-Page results for sample 10E003B4433 show? Were the SDS-Page results necessary to be able to confirm sample 10E003B4433 as an adverse analytical finding for CERA in accordance with WADA's Technical Document TD2009EPO?*

Figure 7 shows the SDS - PAGE gels as provided by the Rome laboratory. The yellow rectangle shows the region of interest for Figure 8.

The SDS – PAGE gel shows a weak band in close vicinity to the CERA standards (see red arrow in Figure 7 and Figure 8). This band is not located on the intersection line of the two CERA bands to the left and right of the sample lane (see blue arrow in Figure 8).

Figure 7 - Region of interest including the CERA standard lanes on the left and the right side of the athlete's sample

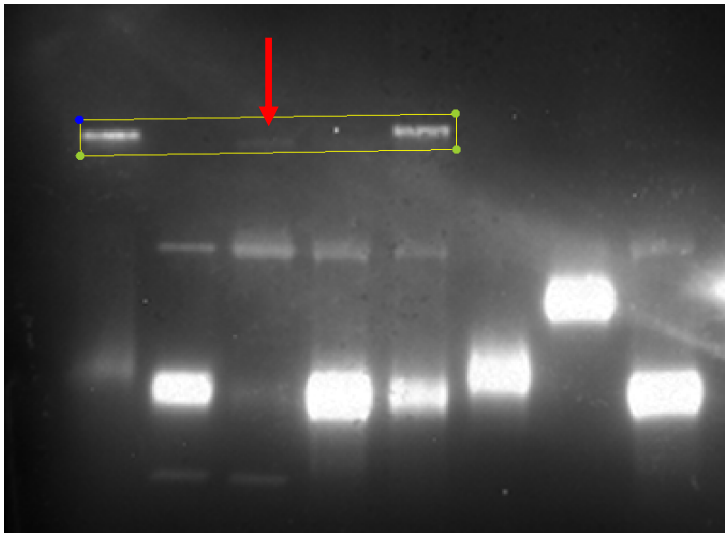
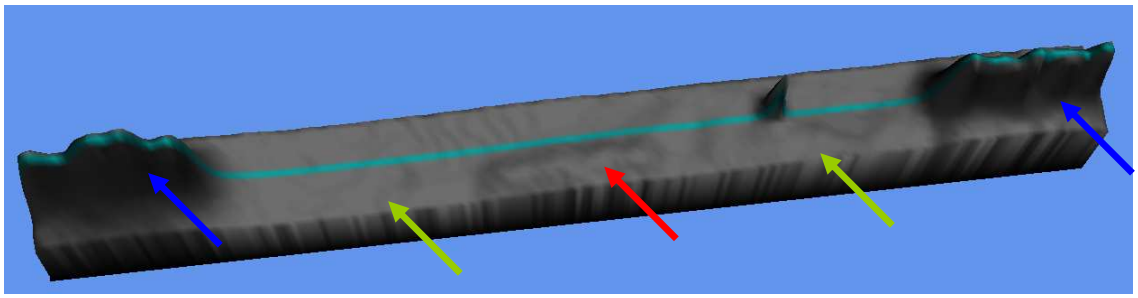


Figure 8 shows a three-dimensional image of the region of interest in Figure 7. Five lanes are included on this figure:

- red arrow: athlete's sample
- green arrows: blank samples left and right to the athlete's lane
- blue arrows: CERA reference standard

The image is a screenshot from the GASepo software tool.

Figure 8 - three –dimensional view of the region of interest as described in the figure above. The lane of the athlete shows a weak shifted band (see red arrow). No band is visible on the left or the right lane next to the sample lane (green arrows). The two CERA standards are indicated by blue arrows.



As can be seen in Figure 8, the blank samples to the immediate left and right of the athlete's lane do not show any sign of a weak band, as can be seen on the athlete's lane (red arrow). This contradicts the opinion of the athlete's experts, which claim to have the same weak band in the blank samples next to the athlete's sample lane.

The spot on the blank sample lane next to the athlete's sample does not have the shape of a band and comes most probably from a protein remainder of the non-fat milk blocking procedure.

Whilst the SDS-PAGE result could be clearer with respect to the presence of CERA in the sample, it does not in my opinion exclude the presence of CERA either. In general, as I have stated, SDS-PAGE is not the recommended method for assisting in the confirmation of CERA. Instead of SDS-PAGE, SAR-PAGE is recommended by our laboratory to confirm CERA due to its enhanced limit of detection. According to the documentation packages, SDS-PAGE was not performed on the A–sample before reporting an adverse analytical finding in this case. Therefore, the Rome laboratory did not need SDS – PAGE data for reporting the A-sample positive.

The second opinion of Dr. Lasne of the A-sample did not require additional evidence by SDS-PAGE either.

As a conclusion, we can state that the SDS PAGE is not required according to the TD2009EPO to confirm the presence of CERA in urine samples. We can also state from the SDS PAGE results that the presence of CERA cannot be excluded from the sample of interest.

8. From your review, did the Rome Laboratory commit any breaches of the International Standard for Laboratories or of any other relevant rule or policy in analyzing sample 10E003 4433 which could have caused the adverse analytical finding in Mr Tysse's case?

After reviewing the documents, I found no indication that the Rome laboratory breached any of the requirements of the International Standard for Laboratories in its current version which may have caused the adverse analytical finding reported by the laboratory.

8.1 Was the storage and handling of sample 10E003 4433 properly conducted (see section 9.2 of MrTysse's Appeal Brief)? Is there any evidence in the analytical material that the stability of the sample was compromised?

There is no evidence in the documentation package that the laboratory did not follow the recommended procedures for the proper storage of the sample concerned.

A stability test was conducted for both the A and the B sample confirmation analyses and in both cases there was no indication of instability.

In any case, I am not aware of any indication that improper storage conditions in terms of temperature may cause an adverse analytical finding for CERA; improper storage might rather be expected to lead to a destruction of the proteins in the sample.

8.2 Did the Rome Laboratory breach section 5.2.4.3.1.4 of the ISL when, at the initial screening stage, it repeated the screening analysis on the same aliquot (see section 10.1 of the Appeal Brief)?

The respective ISL section 5.2.4.3.1.4 relates to the confirmation analysis procedure and not to the screening analysis. This paragraph therefore does not apply to the procedure performed by the laboratory.

The purpose of screening data from the initial testing of a sample is to provide a clear differentiation between negative and potentially positive samples. Initial testing procedures can be repeated in whole or in part as long as the repetition is recorded and documented. Extracts or retentates can be repeatedly used for a new instrumental or IEF analysis. The ISL has no restriction for such a procedure and the Rome laboratory therefore committed no breach of the ISL in this regard.

8.3 Did the Rome Laboratory breach the ISL documentation and reporting requirements (see section 10.2 of the Appeal Brief)?

I found no indication from my review that the Rome laboratory has breached any ISL documentation or reporting requirements. In my opinion, the evaluation of the results was done properly and is documented.

9. Please comment briefly on the statements made by the experts of Mr Tysse in Appendices 13, 16 and 19 of the Appeal Brief. Do you agree with their respective conclusions?

<u>Modification of the EPO profile as a function of time; destruction of the sample:</u>

The athlete's defense experts claim that the difference between the initial screening of the particular sample and the subsequent screening as well as confirmation analyses demonstrate clearly that the urine sample was destroyed during storage as demonstrated by the disappearance of the endogenous EPO bands. I do not agree with this statement for the reasons stated below.

It is true that the initial screening shows more intense bands in the endogenous area compared to the subsequent analyses. It is also true however that the initial screening gel shows clearly that the bands in some lanes are merged in-between the lanes. This effect can be a consequence of the use of applicator strips which occasionally leak and it cannot be excluded that lane 3 was contaminated with retentates from the neighboring lanes. This is one possible explanation for the increased intensity of bands in the endogenous area.

In any case, due to quality issues, the data from the first screening was not accepted by the laboratory and the IEF analysis was repeated from the same retentate. Consequently, the data from this initial screening was nullified and the data from the second screening was considered as the valid data for assessment purposes.

The data from the second screening and the A-sample confirmation, as well as from the second, repeated B-sample confirmation show a similar intensity distribution in the endogenous area compared to the basic area, where bands appear which were interpreted to derive from CERA.

In addition, the laboratory performed a stability test with the respective sample during the confirmation analysis which gave no indication of possible instability of the EPO–isoforms present in the sample.

Finally, the percentage of endogenous bands compared to all bands in the entire lanes of the sample in the gels accepted by the laboratory (i.e. second A-sample screening, A-sample confirmation, second B-sample confirmation) is comparable and in the low percentage range.

Criteria of the Technical document

The gel image fulfills the criteria of the WADA Technical Document in terms of acceptance, identification and stability. No other explanation than the presence of CERA can be given for the analytical data presented by the laboratory.

Second B-sample Confirmation

The second B-sample confirmation shows a band distribution with a slightly different intensity pattern compared to the previous analyses. The bands are located in the area where CERA is to be expected. Slight shifts of the bands compared to the standard lanes are normal and depend on factors like the protein load of the sample as well as the homogeneity of the gel cast by the laboratory. The second analysis of the B-sample can therefore be regarded as a confirmation of the A-sample analytical data.

Criticism of GASepo

The criticism issued regarding the GASepo software was in the form of a letter to the editor, which was not peer-reviewed. The criticism was globally without any concrete focus and does not present any evidence of what is the target of the criticism.

On the other hand, it has already been mentioned that GASepo is a validated software, the algorithms are published in a peer-reviewed form and the software is accepted by WADA for image evaluation (vide infra).

Weak band on the lane of the blank sample

As mentioned above, and as can be seen on Figure 5 of this document, a weak band (red arrow) appears in the lane of the athlete on the SDS PAGE image, located close to but not on the intersection of the two CERA standards at the respective reference lanes (blue arrows). There is no band visible in the lanes of the blank samples to the immediate left and right of the athlete's lane (green arrows) close to the band in the athlete's sample.

This contradicts the opinion of the athlete's experts which claim to have the same weak band in the blank samples next to the athlete's sample lane.

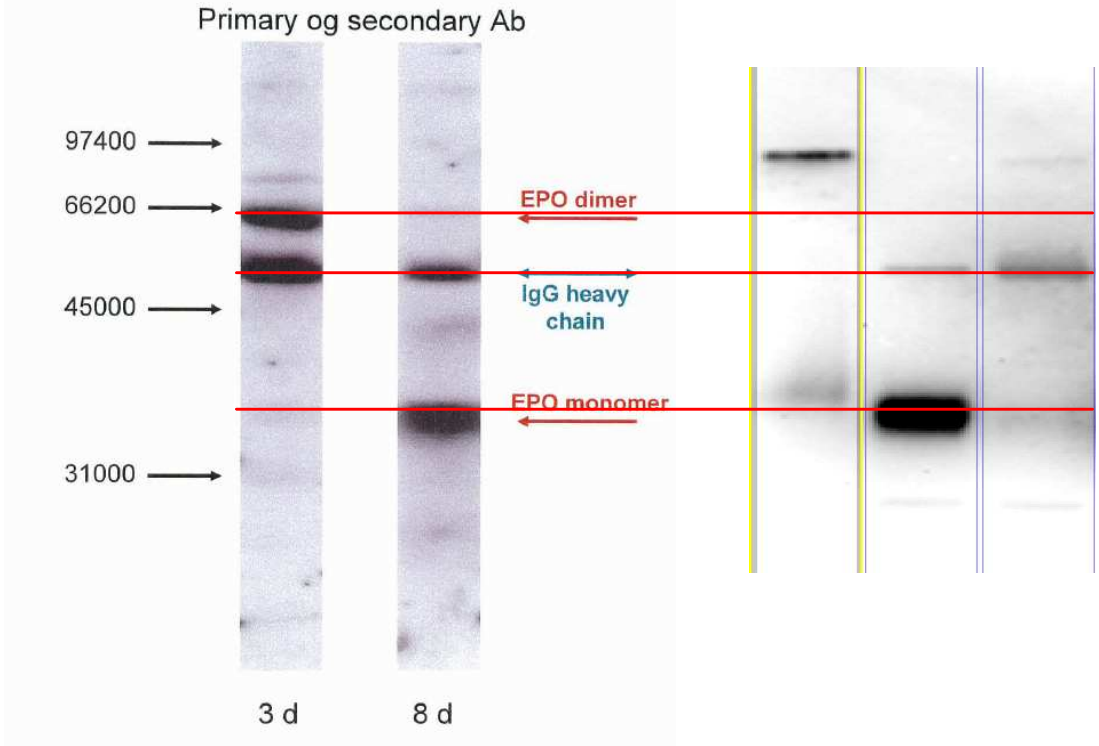
Band appearance after Iron injection

The adverse analytical finding is based on IEF PAGE. SDS PAGE was not regarded necessary to report the adverse finding for CERA in this sample. Proof with a traceable experiment that iron injection may cause a band pattern similar to CERA on IEF PAGE has not been provided by the athlete's defence.

Presuming the same analytical setting as in Rome, the SDS PAGE experiment performed by the athlete's expert showing a possible dimerisation of endogenous EPO as a possible reason for the band with a similar mobility value as the CERA reference substance in fact demonstrates the contrary: dimerisation is most likely not the cause of the band.

This is demonstrated in the following figure.

Figure 9 - Comparison of the gel from an experiment performed by the athlete's experts and an extract of the SDS PAGE gel image from the Roman laboratory containing the athlete's sample on the very right side.



Left:	Right:
Image copied from appendix 13 of the athlete's appeal	Image showing from left to right a reference lane, a blank sample and the athlete's sample

The position of the EPO – monomer, the IgG heavy chain, as well as the proposed epo-dimer from the experiment of the athlete's experts, was linked to the respective lanes of the SDS PAGE analysis containing the athlete's sample on the very right side. The SDS PAGE gel from the Rome laboratory containing the athlete's sample does not show any band in the position where the proposed EPO dimer should appear according to the gel image on the left side of Figure 9. If the band indicated as an EPO – dimer in the experiment of the athlete's expert represents a dimeric form of urinary EPO of human origin, than this band is absent at the mobility position of the athlete's sample. Consequently, no indication for a possible "dimerisation" of uEPO is given by the analytical data.

No indication of the formation of a possible EPO-trimer, as alternatively assumed by the athlete's defense in addition of being a dimer, is visible on the gel image of the experiment (Figure 9, left side), either.

10. Could there be any other explanation than doping for the presence of bands in the CERA region in Mr Tysse's sample 10E003 4433?

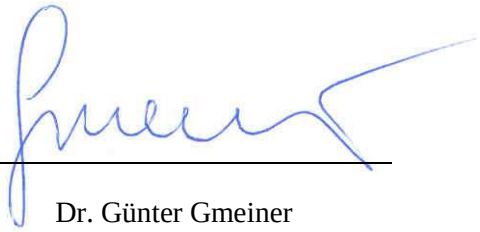
According to our experience in the detection of recombinant forms of erythropoietin and, according to the review of several thousands of samples, predominantly from sports disciplines where rEPO may cause a performance enhancing effect (cycling, triathlon, athletics, etc.), including samples from major games like the Olympics, we can clearly state:

- **That the band pattern and isoform distribution of the sample corresponds to the pattern of the CERA standard substance, as seen in parallel on the A sample screening as well as on both the A and the B sample confirmation gels.**

- **That the data presented complies with the criteria of positivity for CERA according to the TD2009EPO**

- **That an analytical artifact derived from a dimerisation of erythropoietin has never been witnessed in our lab.**

Taking into account the above, in my opinion, there is **no other explanation** for the analytical data **than the presence of CERA in the athlete's sample**.



Dr. Günter Gmeiner

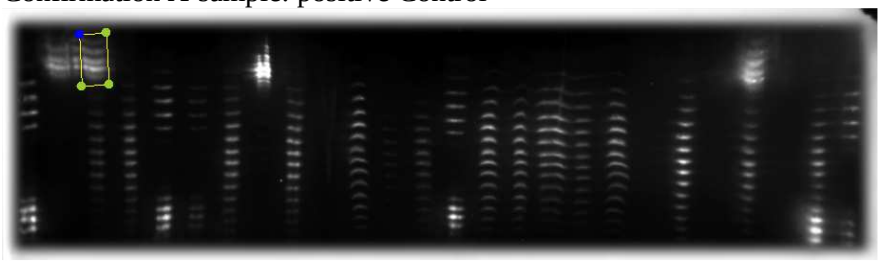
2011/6/22

Date

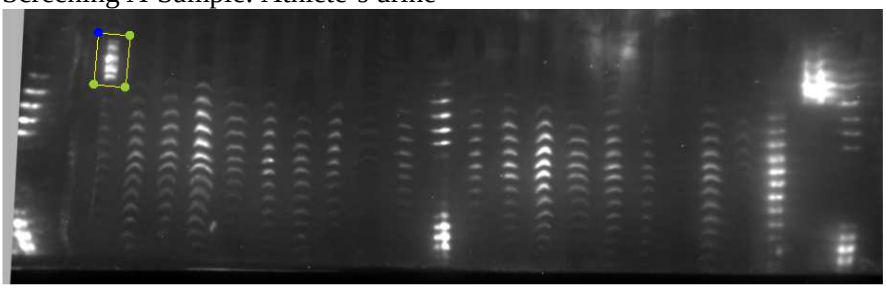
Addendum:

Figure 10 – Regions of interests (yellow rectangles) relating to the images in Figure 4, black and white colors reversed to Figure 3

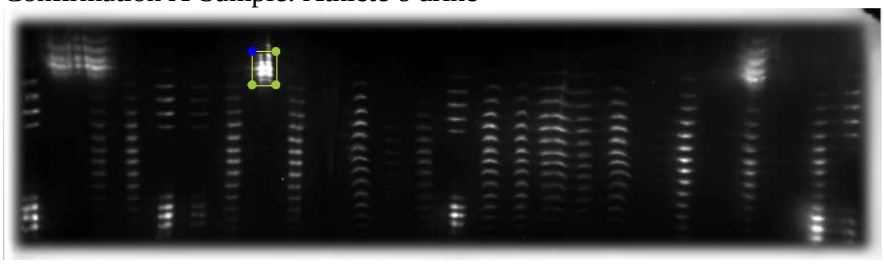
Confirmation A-sample: positive Control



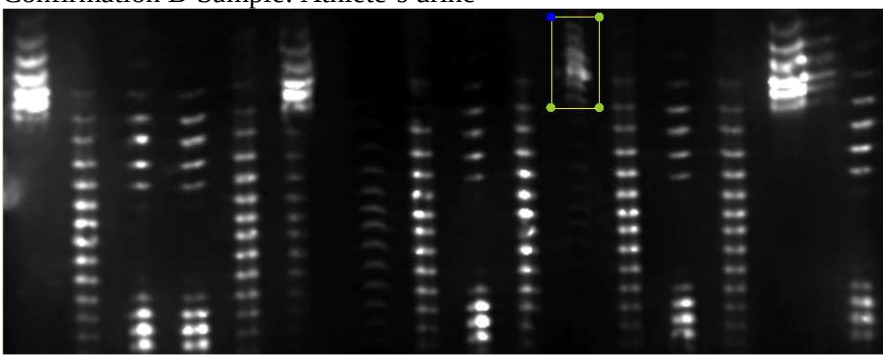
Screening A-Sample: Athlete's urine



Confirmation A-Sample: Athlete's urine



Confirmation B-Sample: Athlete's urine



Confirmation B-sample: positive Control