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Anti-doping : from health tests to the athlete biological passport

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Running Title : Beginning of ABP

Abstract

Athlete biological passport (ABP) was implemented in International Cycling Union (UCI) in 2008. However, this improvement in the fight against doping was preceded with different milestones since 1996.

In this paper, a detailed evolution of the ABP out of traditional direct (urine) testing for anti-doping purposes is presented. Chronological overview of the ABP including earlier non-disclosed information and contemporary documentation are shown and documented. The strategic development from on-site competition blood testing, called “health tests”, to the structure of the ABP is explained in this historical overview which provide information to the anti-doping community and general public regarding the beginning of blood doping tests.

The history of blood sampling in anti-doping

Historically, urine was the only body fluid used for doping control purposes. In the 1980s, various sports authorities recognised that the use of autologous and homologous blood transfusions to increase the endurance performance of athletes was a major threat to the integrity of the sport. Subsequently, the medical commission of the International Olympic Committee banned blood doping and the collection of blood samples for doping control became necessary. Because the misuse of endogenous substances such as erythropoietin (EPO), human growth hormone and testosterone was very difficult to detect in urine, the idea that blood sampling would enable reliable detection of such substances became more widely accepted.

In 1989, the Medical Commission of the International Skiing Federation (FIS) started collecting blood samples for doping control purposes, although there were no clearly defined legal regulations at the time. Initially, the sports community thought that the collection of blood samples for doping control would not be feasible for cultural, religious or legal reasons; however, in 1992 the International Association of Athletics Federations (IAAF) decided to conduct blood tests during major meetings of the seasons of 1993 and 1994 [1, 2]. Though proof of blood doping could not be obtained at the time, a number of hormone concentrations and haematological parameters were measured, albeit without any legal actions following the tests. Nonetheless, the principle of blood collection during major competitions in the context of anti-doping was accepted.

In 1993, prior to the 1994 Winter Olympic Games in Lillehammer (Norway), Peter Hemmersbach (director of the anti-doping laboratory in Oslo) and his colleague Käre Birkeland organised the Second International Symposium on Drugs in Sports, entitled “Blood Samples in Doping Control” [3]. At the time, recombinant human EPO (rhEPO) was on the market since 1989. Thus, the session on blood doping and EPO misuse was of particular importance. Several groups presented proposals to solve the problem based on measuring a number of biological markers in blood samples, which was completely unusual in doping controls at the time. The group of Professor Conconi, an internationally recognised specialist in erythropoiesis and the physiology of endurance athletes, had proposed already earlier several markers of erythrocyte morphology, including an increase of hypochromic macrocytes

after rhEPO administration [4]. One of the most interesting reports was the use of several markers associated with the biological cascade of erythroid maturation to detect EPO doping, a method developed by a collaborative team from Canada and France [5]. Of these markers, the soluble serum transferrin receptor (S-TFR) seemed to be the most sensitive to EPO doping [5] and the authors published a letter in the journal *Nature* stating that the most reliable biomarker to detect EPO abuse was the sTFR/ferritin ratio in blood [6].

The introduction of health tests in cycling

The Food and Drug Administration (FDA) approved the use of recombinant EPO to treat severe anaemia and kidney deficiency in 1989. Since then, the misuse of this medication by athletes, with the goal of improving their endurance capacities, has increased exponentially. In the 1990s, it was recognised that the misuse of EPO and blood doping in general was of major concern not only to cross-country skiing and endurance disciplines in athletics, but also to cycling. The Medical Commission of the International Cycling Union (UCI) was aware of this fact due to rumours from the cycling community, as well as some unexpected performances of certain cyclists.

In January 1996 Dr Lon Schattenberg, the medical director of the UCI, called a meeting with the directors of several anti-doping laboratories to discuss hot topics in anti-doping, including the misuse of EPO. At the time, all anti-doping tests were based solely on urine samples collected in competition. During the discussion, a meeting was proposed to be held with Canadian researchers to evaluate the utility of blood anti-doping tests. Consequently, the meeting occurred in Brussels Airport between the UCI (Hein Verbruggen, the UCI president), the Canadian researchers and representatives of the Lausanne laboratory to discuss the implementation of blood tests in cycling. The situation regarding EPO abuse was considered critical. Some top level cyclists urged the UCI to develop a method for the detection of EPO misuse, noting that the lack of a variable test would lead to serious damage to the health of the riders, the image of cycling and the fair play of the competition. It was clear to the cyclists that the misuse of EPO was not comparable to the amphetamine doping that occurred in the 1970s, as it completely changed the configuration of the races and the performance profile of the cyclists. For example, a good climber could suddenly become a good time trial specialist. EPO changed the world of cycling to the extent that every teammate was obliged

to use it to support his leader. These considerations likely formed the basis of the wish of both the president and the medical director of UCI to communicate strong message of deterrence and prevention against this epidemic threat.

The medical director of the UCI was originally a specialist in occupational medicine; consequently, he was personally most affected by the exposure of a sports professional (in this case, a cyclist) to a health risk. It was known that for an athlete with a natural haematocrit (HCT) of 44%, for example, uncontrolled EPO treatment could raise it to more than 55%, sometimes even to 60%. Also most cyclists abusing EPO had to wake up in the middle of the night to circulate their blood by performing push ups and prevent their heart stopping due to high blood viscosity. Consequently, although the image of the sport was certainly a concern for them, the UCI committed to preventing EPO doping primarily for health reasons.

In 1996, the Swiss Laboratory for Doping Analyses and Canadian researchers (Gareau et al.) contacted the UCI to propose a protocol to determine the prevalence of EPO misuse in a specific population of cyclists. The proposal was based on the use of haematological and biochemical parameters described in the literature at the time, including the biomarkers described in the newly published paper by Gareau et al. [6]. It involved a comparison of sports students before and after a 5000 meter race on the track (control group) and a population of professional cyclists taking part in an official UCI stage road race (test group). For the test group, blood samples were collected from riders taking part in the Tour de Romandie in May 1996. A written agreement was concluded between the UCI, the Association of Professional Teams and the event organiser to ensure that blood collection was performed in a professional environment after the prologue in Basel. Two teams (five riders per team) were tested; however, the legal representative of the International Association of Professional Cyclists (AICPro) travelled from Milan and stopped the procedure because none of the cyclists involved in the Tour de Romandie had given their informed consent. The team of researchers were asked to destroy the blood samples that had already been collected and the principal investigator of the protocol (Dr Saugy) was invited to an ad hoc meeting with the cyclists in a hotel in Basel. The meeting was chaired by the legal representative of the AICPro, whereas other officials (including coaches, UCI representatives, physicians and event organisers) were excluded. Dr Saugy was asked to explain the main goals of the protocol and to focus on the

academic value of the experience rather than the potential development of an anti-doping rule. Unsurprisingly, most of the questions from cyclists were related to the potential health risks of using doping agents and the necessity to treat every rider equally. The main concern of the riders was what could be detected in the blood samples, whether the analyses could provide clear evidence that a drug was used and whether they could be sanctioned because of the blood test results. The cyclists also expressed concerns over the result management whether the UCI would receive open or anonymised results. Overall, Dr. Saugy felt that the meeting was very tense but gave a clear picture of the concerns and questions of equity held by the peloton at the time.

Subsequently, a decision was made to proceed with the experiment during the ten-stage Tour de Suisse in June 1996. The protocol was negotiated and finally approved by the president of the AICPro, and the agreement between all parties became effective at the beginning of June 1996 **(Figure 1)**. Blood samples were collected from the riders during the fourth and seventh stage, after they had returned to the hotel at the end of the stage and before their evening meal. In all cases, blood sampling was performed between 45 minutes and 2 hours after completion of the stage. The fourth stage was described as relatively easy and flat (Bienne-Bussigny/Lausanne, 190 km), whereas the profile of seventh stage was more steep and difficult (Ascona/Grindelwald, 198 km). Seventeen teams participated in the Tour de Suisse and blood samples (EDTA whole blood and serum) were collected from five of the nine riders per team. Only one team did not cooperate. In total, 80 samples were collected. The results of the Tour de Suisse experiment were provided to the medical department of the UCI and were presented to the team physicians and managers in Geneva on 24th of January 1997, and were published in 2000 [7].
Based on the results, it was obvious that no definitive parameter could be used as direct proof of EPO doping. It was concluded that, even if they fell dramatically outside of the natural levels of normal population, none of the parameters measured could be used as strong evidence to justify presentation in front of an anti-doping disciplinary panel. In 1997, the introduction of a “no-start” rule was proposed for cycling competitions, based on a cut-off level of HCT [8]. In fact, the UCI was not the first to impose such a rule; the FIS had made a similar decision several months earlier. During the 1996–1997 season, the FIS performed pre-race haemoglobin (Hgb) measurements and excluded athletes with Hgb levels greater than

185 g/l (men) or 165 g/l (women) from competition. The Geneva meeting made a similar no-start rule decision, but the cut-off was based on the HCT level. The choice of the HCT level rather than the Hgb level was made for didactic and cultural reasons. At the time, all of the riders and their doctors discussed HCT levels routinely and most of the teams possessed a centrifuge, which was required to measure the HCT, and in all likelihood, to titrate the dosage of EPO **(Figure 2)**. The HCT threshold was set at 50% for men and 47% for women. These limits correspond to the 95th percentiles of the normal male and female populations, whereas the value of 53% corresponds to the 99th percentile of a normal male population [9]. Due to the uncertainty of the measurements, the decision limits (threshold + uncertainty factor) were in fact set to 51% and 48% for males and females, respectively. However, during a meeting with the team physicians, the debate was quite controversial. Some of the teams argued that the HCT value of 53% should be considered as the normal range according to their hospital standards. Finally, a 50% threshold was adopted. This threshold was not considered a new anti-doping rule, but was rather a competition rule and part of the medical regulations, which justifies its qualification as a "health test" at the beginning of the campaign.

The first HCT test was performed at the "Course au Soleil" Paris-Nice in 1997. Prior to the start of the race in Paris on March 9th, blood tests were performed on several riders in their hotel. Two riders had HCT values higher than 51%. The procedure was as follows: one tube (4 ml) of EDTA blood was collected and two analyses were performed using a transportable automated haematology analyser (Coulter ACT) installed in a conference room. If the HCT result was higher than 50%, the analyses were repeated five times and the mean value was calculated. If the mean value was higher than 50 + 1%, centrifugation was performed to validate the results. Then, if the overall result exceeded 51%, the rider would be declared non-eligible for the race **(Figure 3)**.

The medical aspect of the HCT test obscured quickly obscured and the term "no-start rule" predominated. The phlebotomists were described as "vampires" of the peloton; regardless of their intents, the medical teams testing the HCT level of riders have been so labelled by their apparent victims in this so-called "drugs-weary" sport.
In 1997, after Paris-Nice, all races were controlled systematically with regard to HCT testing, including the Milano-San Remo, the Belgian Classics, Giro d'Italia, Dauphiné Libéré, Tour de

Suisse, Tour de France, Vuelta a España and the World Mountain Bike Championships (Chateau d'Oex, Switzerland), as well as other track cycling (Perth, Australia) and road cycling (San Sebastian, Spain) events. The approach was initially criticised not only by athletes in the field, but also by the international sport and anti-doping communities. The latter argued that the first big name in cycling excluded from a competition because of a high HCT level measured in the field would easily win the case in front of any arbitration court. In fact, it never happened. The application of this medical rule, discussed many times in the media, was finally accepted because it was a joint decision by the relevant parties and recognised as the application of preventive measure of occupational health.

The methods involved in blood collection and HCT testing have evolved over time. From 1997 to 1999, testing involved the collection and analysis of only one 2.7 ml sample of EDTA whole blood. If the mean HCT value (of two analyses and after subtracting 1%) was above 50% for men or 47% for women, the rider was given the opportunity to be present for the subsequent analysis (mean of five measurements), which was done using the same sample within one hour of the first analysis. Throughout this period, the principal teams of the peloton immediately adapted to the policy. During the famous Festina affair, a series of doping scandals during the 1998 Tour de France, it was already clear that all riders were being closely supervised by their personal staff to ensure that none of the teammates of the team leader were excluded of the race.

In 1998, after the introduction of the hemoglobin or hematocrit limits as a no start rule by FIS and UCI respectively, rumors indicate the use of plasma expanders, mainly hydroxylethylstarch (HES), in order to decrease the hematocrit or hemoglobin concentration values. Another advantage of its use for the endurance performance was the increase of body fluid preventing any dehydration in exercise.

The use of HES has shown its apex at the World Championships of Nordic Skiing in Lahti, Finland in February 2001, where it became evident that the use of HES was certainly to cover EPO doping. Administration of HES allowed for circumventing the FIS no-start rule by diluting the blood and hemoglobin values.

The skiers were also not aware of the fact that since January 2000, HES has been introduced into the IOC doping list and that the Cologne laboratory had just published a method for the detection of HES in urine [10], without making it largely public.
Then, at "their World Championships" in Lahti, six Finnish skiers tested positive for HES, giving rise to a huge scandal in their country and in Scandinavia in general where cross country skiing is considered as one of the national sports. It can be noticed that this event was also the first one which involved the implication of the newly formed World Anti-Doping Agency [11].

During one of our on-site blood missions in 1998, a Coulter analyser was found installed in the hotel conference room of one of the teams. A discussion with the team doctors revealed that all major professional teams had decided to buy a Coulter ACT analyser at the beginning of the season to ensure agreement with the HCT values measured on the morning of each race by the UCI medical team.

In 2000, the HCT testing procedure was made more robust, professional and transparent. The calibration procedure of the on-site apparatus was available to the riders and team doctors. That year was also a period during which on-site blood analyses "missions" were conducted during competitions. All instruments required for blood analyses were transported from the laboratory to the competition site by a private plane **(Figure 4)**. Overall, 28 missions were performed across Europe in 2000 **(Figure 5)**.

As part of the decision to make the blood testing procedure more robust, an Hgb limit of 17 g/dl (for an HCT value of 50%) was proposed. Moreover, two blood samples (A and B) were collected from each rider and all "B" samples from the same team were put in a sealed container signed by the team doctor. In the case of an "A" sample that failed due to HCT/Hgb levels above the cut-off, this container was opened in front of the team doctor and/or the rider. The "B" sample was analysed twice and if the HCT and Hgb values were still above the cut-off levels, a manual measurement of the HCT level was performed by centrifugation **(Figure 6)**. If the centrifugation result confirmed that the HCT value was higher than 50%, then the no-start decision was formalised by the UCI commissioner and reported to the rider and team doctor. The rider was then unable to compete for a further two weeks, after which he/she had the right to go back to a UCI-certified laboratory to undergo the same test to check

that the HCT value was lower than the cut-off. The HCT value was naturally elevated and constantly higher than 50% in only a few cases. Those riders were able to obtain a certificate of naturally elevated HCT and Hgb after proper investigation by the haematology department of a university hospital. All files from these investigations were examined by an independent commission to ensure that the result was not the consequence of a manipulation.

During the Tour de Suisse in 1999, another study was conducted to advance with the development of the blood testing system and to determine whether additional biomarkers could be used to detect doping. At that time, various blood counters were commercially available and their abilities to obtain a more complete blood profile were tested. The results of these tests were published in 2000 by Robinson et al. [7]. At the time, all cyclists (n = 146) were required to give a blood sample before the start of a single stage. The HCT and other parameters related to erythropoiesis, iron metabolism and liver function were measured. In 1999, a method for detecting EPO in urine did not exist yet, but the abuse of the substance in cycling (and other sports) had been discussed widely in the media following the scandal of the Festina affair at the 1998 Tour de France. A narrow HCT distribution was observed in some teams and more than 50% of the cyclists had ferritin levels higher than 300 ng/ml. Most of the ferritin levels were also related to the same teams. Importantly, the reticulocyte indices (absolute count, percentage and immature reticulocyte fraction) showed large inter- and intra-team variabilities. This high variability was attributed to manipulations of erythropoiesis, including non-prohibited methods such as altitude training or hypobaric chamber sessions, but mainly involving the prohibited and undetectable use of recombinant human EPO.

In 2000, several groups published important papers regarding the problem of EPO doping. In the French anti-doping laboratory in Chatenay-Malabry, de Ceaurriz and Lasne published what can be considered as one of the landmark studies in the fight against doping at the time, a proof of principle study related to the detection of recombinant EPO in urine [12]. In parallel, a group of scientists in Canberra was studying the problems related to EPO abuse detection using an indirect method that included the measurement of several blood parameters. Consequently, the concept of “on-score” (meaning on EPO treatment) and “off-score” (meaning off EPO treatment) was established [13]. Subsequently, the International Olympic Committee decided to use a combined method of direct detection in urine and indirect

detection in blood to test competitors in some endurance disciplines during the 2000 Summer Olympics in Sydney. No positive cases resulted from these tests nevertheless there were a good start for the use of blood tests to screen for possible manipulations and to target athletes for EPO testing in urine.

In 2001, the Lausanne Laboratory implemented the EPO test upon need of UCI and the analysis of the reticulocyte percentage using Sysmex technology was adopted **(Figure 1).** Detection of significantly elevated reticulocyte percentage in a blood sample triggered the subsequent collection of a urine sample for EPO analysis. During the Belgian Classics in 2001, this approach led to the identification of the first two adverse analytical findings for EPO. Despite the earlier criticism against the direct EPO method, its importance is recognized and applied to the testing strategies in endurance sports by the technical document for sport specific analyses. In addition to the UCI, the FIS and IAAF introduced the EPO test in 2001 and use blood tests (mainly the Hgb level, HCT level and percentage of reticulocytes) for the initial screening.

The introduction of reticulocyte percentage measurements into the blood health tests as a method of screening for targeted candidates for the EPO urine test caused a dramatic change in the behaviour of cyclists and other endurance athletes. Typical reticulocyte percentages throughout 2001 and 2003 clearly showed a change in the athlete population **(Figure 7)**. Low or very low reticulocyte percentages were typically observed in 2003, suggesting the use of blood transfusions, certainly in parallel to EPO micro-dosing. Furthermore, the feedback regulation of reticulocyte production caused by blood transfusion was clear and dramatic in some cases. The very high intra-individual variability in the reticulocyte percentage of some individuals was an important indicator of the combined use of transfusions and EPO micro-doses**.** Rumours of such a change of paradigm soon reached also anti-doping scientists. It seemed at the time that both autologous and homologous transfusions were being used.

In 2003, Nelson et al. [14] developed a test capable of detecting a mixed red cell population by utilizing flow cytometry and the likelihood of differences in minor blood group antigens. At the end of 2003, the World Anti-Doping Agency (WADA) supported a project to transfer detection method to the anti-doping community. In Lausanne laboratory, Giraud et al. worked on the project and established standards for the method, which was implemented in

both the Lausanne and Athens anti-doping laboratories prior to the 2004 Olympic Games [15]. At least two athletes were sanctioned for doping with homologous transfusion in 2004. Studies on the finding revealed a dramatic decrease in typical reticulocyte percentages immediately prior to the Olympic Games and major cycling tours. At the same time, the idea to use the compiled blood data of athletes for individual and longitudinal follow-ups started to be adopted by the anti-doping community.

Development of the athletic biological passport

A project supported by the WADA and UCI was accomplished by the Lausanne anti-doping laboratory to create a biological passport that utilised the enormous amount of blood data collected from the athletes in cycling and athletics communities [16]. An example of the data collected for an athlete convicted of homologous blood transfusion was reported by Giraud et al. in 2010 [17] and is shown in **Figure 8**. The athlete was using homologous transfusions for approximatively 6 months [17]. The drastic elevation of the Hgb level, highly significant suppression of the reticulocyte percentage and off-score completely outside of the limits supported strongly the scenario of the use of blood transfusions. Of course, at the time, the legal basis of the athlete biological passport was not yet established ; however, because the transfusions were homologous (rather than autologous), it was possible to prove the manipulation and the presence of foreign red blood cells by flow cytometric analyses. If the transfusions had been autologous, flow cytometric analysis would have not provided the existence of adverse analytical findings.

The blood transfusion case had certainly an impact on the decision to establish longitudinal follow-ups of blood parameters for individuals. Subsequently, UCI proposed changing the philosophy from direct detection to indirect detection of doping. Until that time, blood analyses were used as a health test that built the basis of the application of a competition rule (no-start rule) [8], although no other type of sanction could be applied. When the urine EPO test appeared, the blood data were used as a screening tool to identify the need for urine EPO analysis. Later, high off-scores were used to identify the potential use of transfusion, which was directly detectable when performed homologous manner.

The indirect approach to the detection of doping and the use of longitudinal follow-up of individual blood test results required also a revision of the anti-doping rules. In the case of an athletic biological passport, violation of the anti-doping rules is not determined by the direct detection of a prohibited substance or method within the biological sample; rather, the passport uses a variety of indirect evidence of the use of prohibited substances or methods to identify doping. Today, various different types of anti-doping rule violations are defined in the World Anti-Doping Code. The drastic difference between the two approaches (direct versus indirect detection) is that, in the case of the passport, the strict liability of the athlete does not apply. It is the responsibility of the relevant anti-doping organization to prove that an abnormal profile or result is due to doping rather than due to a pathological or physiological condition.

Although the detection of blood doping remains a difficult challenge for the laboratories and anti-doping organisations, the haematological module of the athletic biological passport has demonstrated its efficiency as a good targeting tool to detect blood manipulation since its introduction by the UCI in 2008.

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Figure legends

Figure 1. Milestones of blood testing for doping control.

Figure 2. Capillary centrifugation to measure the haematocrit.

A) Example of a capillary centrifuge instrument.
B) Haematocrit result of 49%.

Figure 3. Scheme of blood analysis at the competition site.

Figure 4. Preparation steps for blood testing at competition sites. A) Materials needed for on-site blood testing. B) Transport of the materials by car to the airport. **C)** Loading of materials onto the plane.

Figure 5. List of "missions" performed in 2000.

Figure 6. Analysis of suspicious blood samples using a Coulter ACT instrument. A) A suspicious "A" sample with haematocrit values of 52% and 52.1%. **B)** Confirmation of the suspicious sample via measurement of the haematocrit by centrifugation.

Figure 7. Trends of reticulocyte percentages and off-scores in cyclists from 2001 to 2003. A) The observed decrease in the reticulocyte percentage between 2001 and 2003, likely due to the use of blood transfusions. **B)** The observed off-scores between 2001 and 2003.

Figure 8. Athlete biological passport profile of a case involving blood transfusion. The region between points 5 and 10 represents the 6-month period over which the athlete was using homologous transfusion.

Figure 1

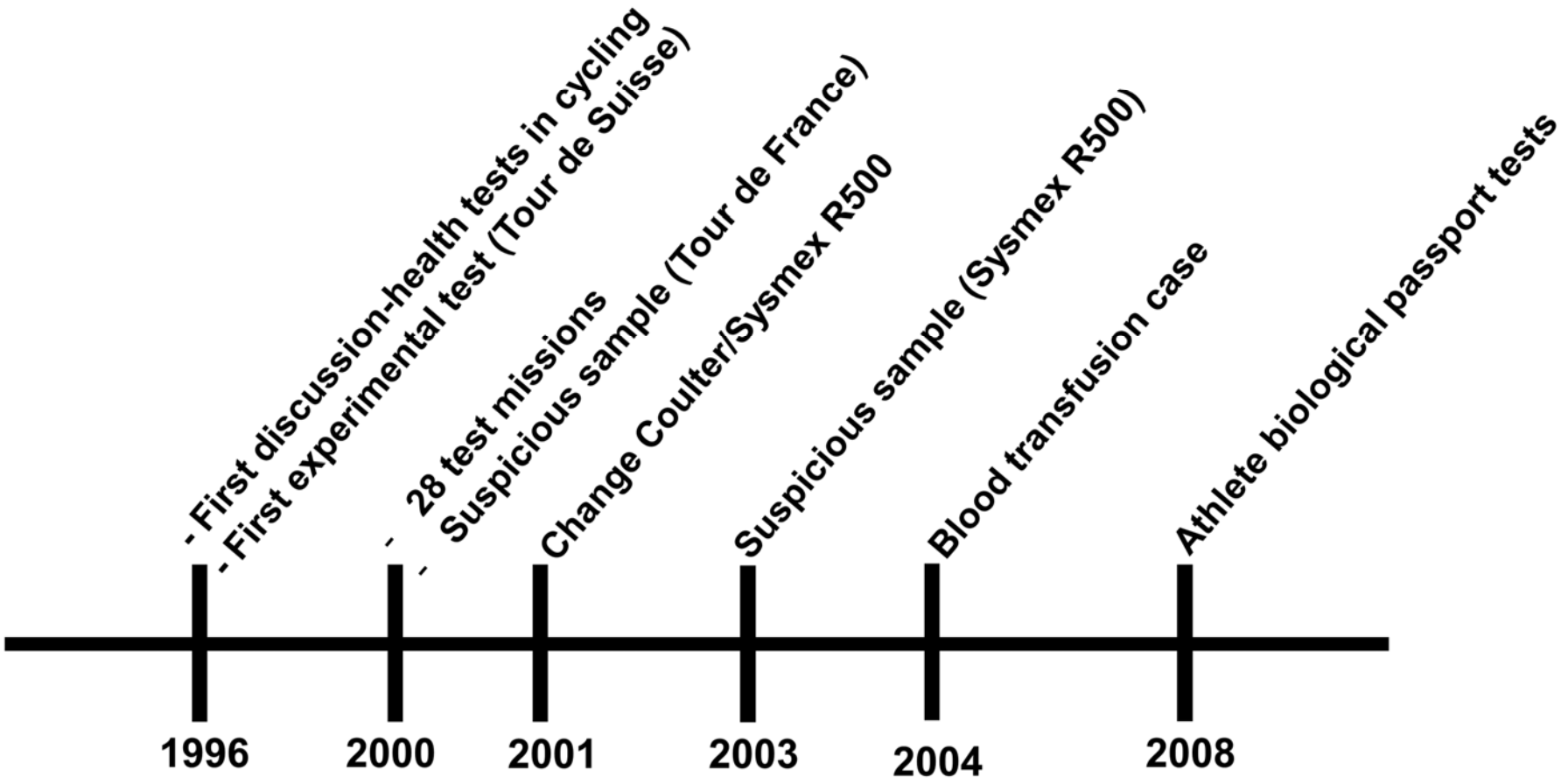

- First discussion-health tests in cycling
- First experimental test (Tour de Suisse)
- 28 test missions
- Suspicious sample (Tour de France)
Change Coulter/Sysmex R500
Suspicious sample (Sysmex R500)
Blood transfusion case
Athlete biological passport tests
1996
2000
2001
2003
2004
2008

Figure 2

A

B

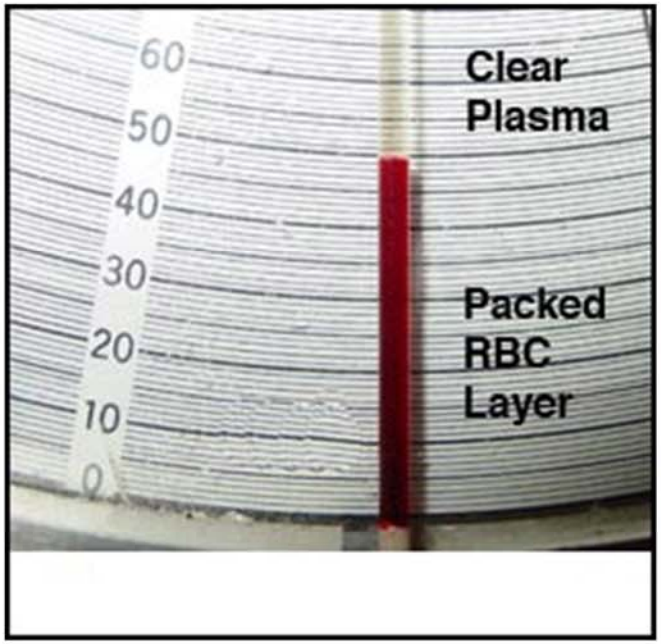


Figure 3

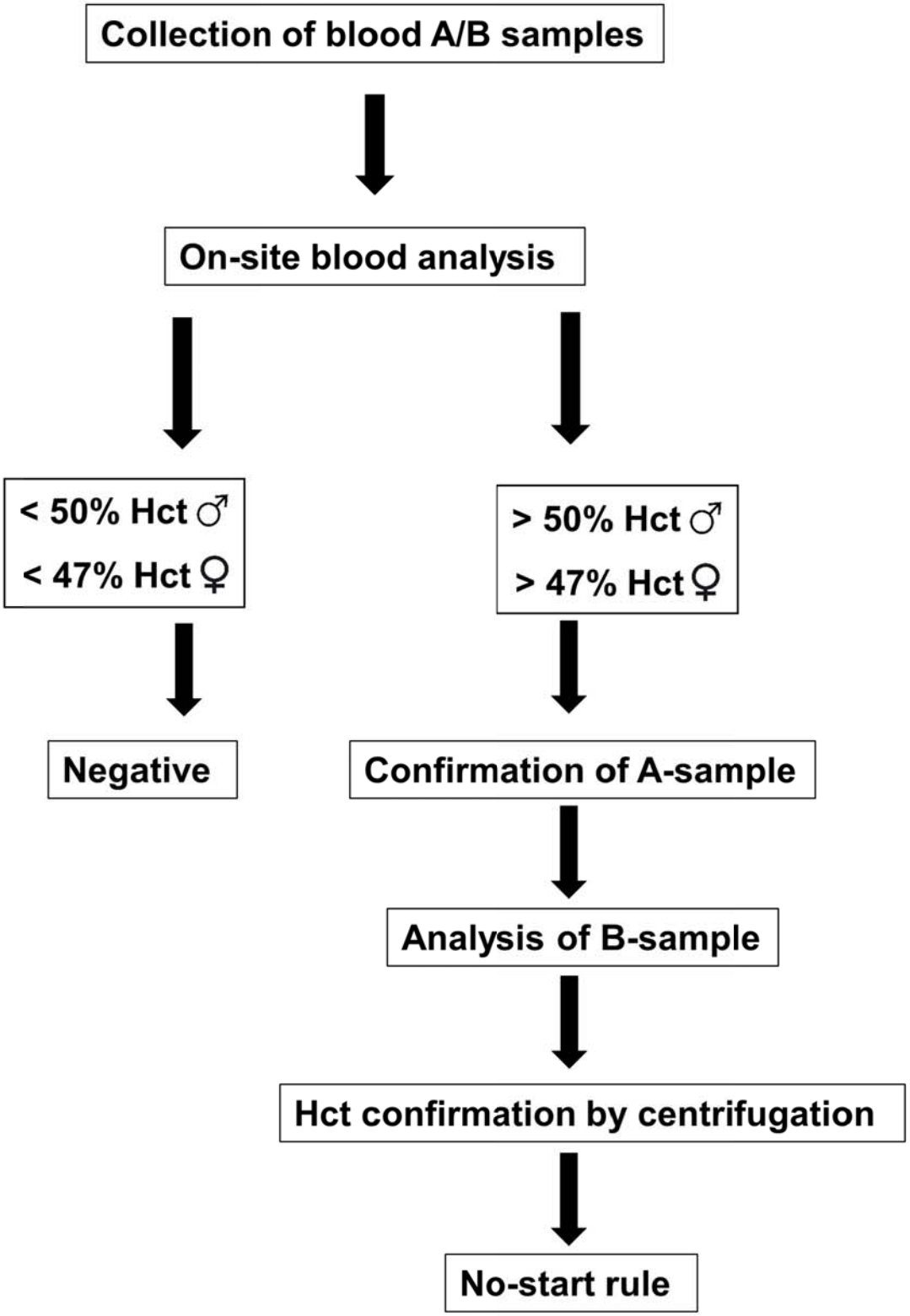

Collection of blood A/B samples
On-site blood analysis
< 50% Hct ♂
< 47% Hct ♀
> 50% Hct ♂
> 47% Hct ♀
Negative
Confirmation of A-sample
Analysis of B-sample
Hct confirmation by centrifugation
No-start rule

Figure 4

A

B

C

Figure 5

Missions	Places	Dates
mission 1	Sint-Michielsgestel	du 27 au 29 janvier 2000
mission 2	Trofeo Mallorca	du 5 au 7 février 2000
mission 3	Tour Méditerranéen	du 10 au 12 février 2000
accréditation et mission	Madrid & Valence + Vuelta d'Andalousia	du 14 au 16 février 2000 prélèvements le 16.02.00
mission 4	Vuelta Ciclista Murcia	du 2 au 3 mars 2000
mission 5	Paris-Nice	du 7 au 8 mars 2000
mission 6	Tirrenno Adriatico	du 12 au 13 mars 2000
mission 7	Critérium International	du 25 au 26 mars 2000
mission 8	Les 3-Jours-de-la-Panne	du 27 au 28 mars 2000
mission 9	Gent Wevelgem	du 4 au 5 avril 2000
mission 10	La Flèche Wallonne	du 11 au 12 avril 2000
mission 11	Mountain Bike World Cup #3 Houffalise	du 29 au 30 avril 2000
mission 12	Tour de Romandie	du 3 au 4 mai 2000
mission 13	St.-Wendel	du 6 au 7 mai 2000
mission 14	Vuelta Asturias	du 10 au 11 mai 2000
mission 15	Giro Italia	du 12 au 13 mai 2000
mission 16	Mountain Bike World Cup #5 Bolzano	du 13 au 14 mai 2000
mission 17	Deutschland Tour	du 29 au 30 mai 2000
mission 18	Giro Italia	du 30 au 31 mai 2000
mission 19	Championnats du Monde Espagne	du 8 au 10 juin 2000
mission 20	Tour de Suisse	du 15 au 16 juin 2000
mission 21	Tour de France Poitiers	du 30 juin au 2 juillet
mission 22	Tour de France Dax	du 8 au 10 juillet 2000
mission 23	Tour de France Morzine	du 18 au 19 juillet 2000
mission 24	Tour de France Lausanne	le 20 juillet 2000
mission 25	Vuelta Espana Malaga	du 25 au 26 août 2000
mission 26	Vuelta Espana Valence et Vinaroz	du 31 août au 1er septembre 2000
mission 27	Mountain Bike World Cup XC # 8 au Chalet-à-Gobet	le 3 septembre 2000
mission 28	Championnats du Monde sur piste à Manchester	du 24 au 26 octobre 2000

Figure 6

A

HEMATOCRITES MESUREES ET CALCULEES PAR L'AUTOMATE COULTER ET LA CENTRIFUGEUSE

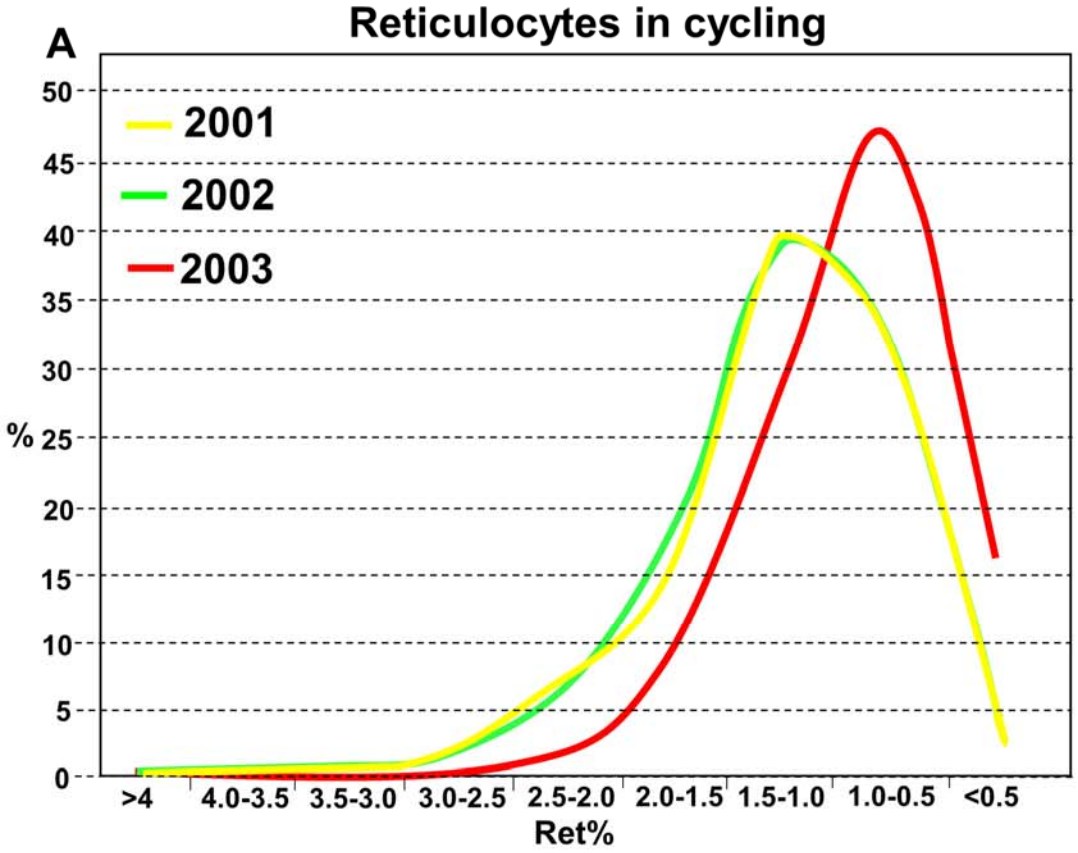
		A (Coulter)				B					
	N° échantillon	Hct 1 [%]	Hb 1 [g/dL]	Hct [%]	Hg 2 [g/dL]	Hct 1 [%]	Hb 1 [g/dL]	Hct 2 [%]	Hg 2 [g/dL]	Hct centri. [%]	Résultat
Team 1	17592	45.4	15.3								
	17585	46.1	15.5								
	17589	44.7	15.0								
	17587	42.2	14.3								
	17586	42.7	14.5								
	17591	46.6	15.7								
	17593	45.7	15.4								
	17588	45.2	15.0								
	17594	46.8	15.7								
Team 2	17599	52,0	17,2	52,1	17,2						
	17600	44,6	14,7								
	17598	45,5	15,1								
	17602	46,7	15,4								
	17603	45,6	15,4								
	17605	49,3	16,7								
	17601	48,0	16,0								
	17604	49,2	16,3								
	17597	45,3	15,1								
Team 3	17647	43,4	14,7								
	17653	44,4	15,1								
	17650	46,9	15,5								
	17654	43,2	14,6								
	17651	49,0	16,3								
	17648	45,1	15,3								
	17649	48,8	16,3								
	17646	49,2	16,3								
	17652	47,8	16,1								

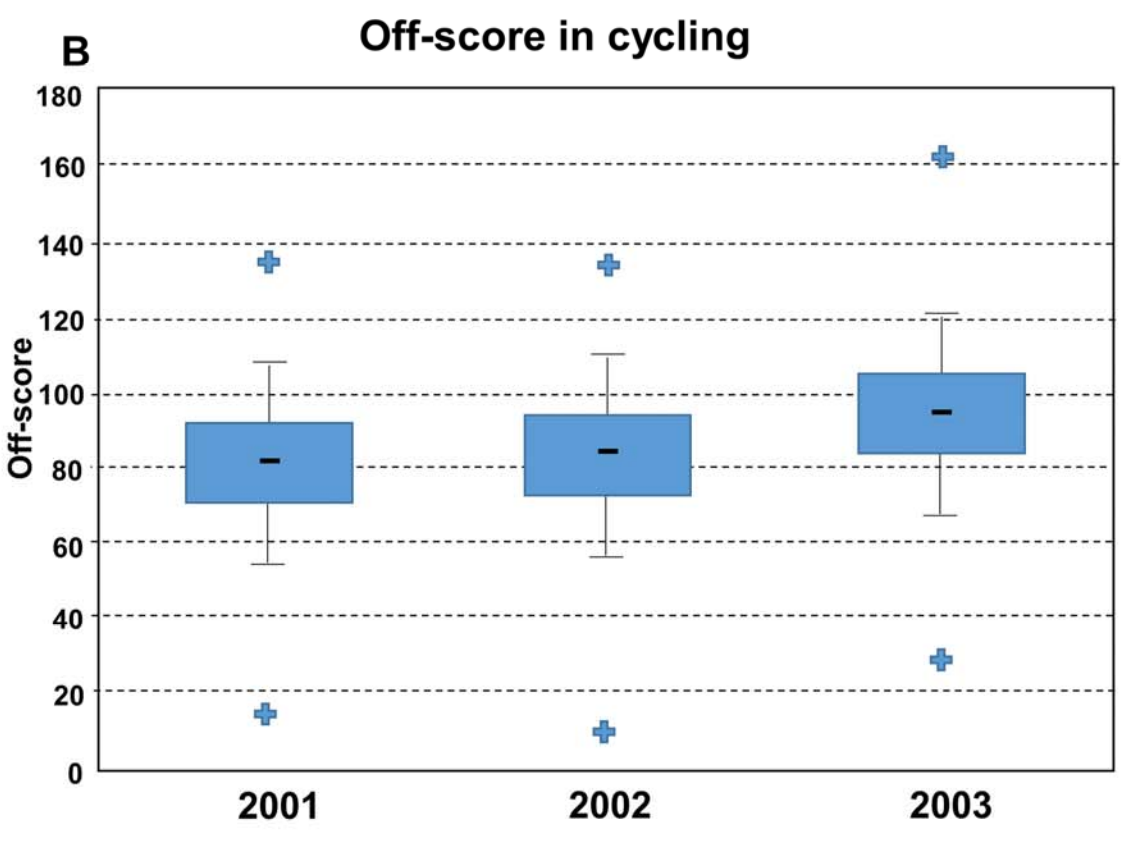
Lieu, date : Pöhlen le 1.07.00. Signature :

B

	A (Coulter)				B					
N° échantillon	Hct 1 [%]	Hb 1 [g/dL]	Hct [%]	Hg 2 [g/dL]	Hct 1 [%]	Hb 1 [g/dL]	Hct 2 [%]	Hg 2 [g/dL]	Hct centri. [%]	Résultat
17599					52,1	17,1	52,0	17,1	52.4	

Figure 7


A
Reticulocytes in cycling
2001
2002
2003
%
50
45
40
35
30
25
20
15
10
5
0
>4
4.0-3.5
3.5-3.0
3.0-2.5
2.5-2.0
2.0-1.5
1.5-1.0
1.0-0.5
<0.5
Ret%


B
Off-score in cycling
Off-score
180
160
140
120
100
80
60
40
20
0
2001
2002
2003

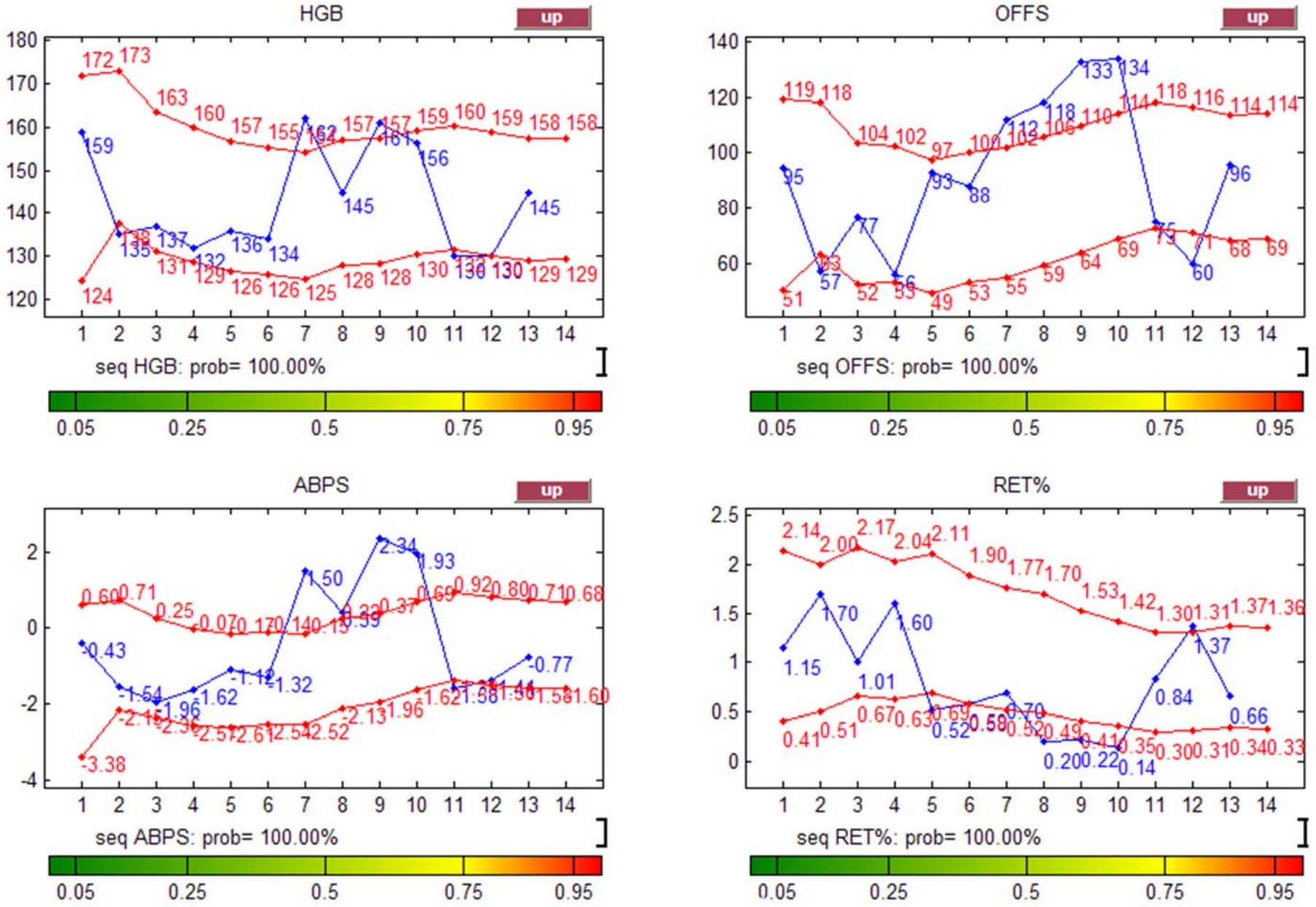

HGB
up
seq HGB: prob= 100.00%
OFFS
up
seq OFFS: prob= 100.00%
ABPS
up
seq ABPS: prob= 100.00%
RET%
up
seq RET%: prob= 100.00%
0.05
0.25
0.5
0.75
0.95

Figure 8