

BVDH e. V. • Coordination Office QA
c/o Die Tastatur Feldstr. 30 52249 Eschweiler/Germany

Ring Trial Prenatal Rapid Test 2018 Final report

Dear Colleagues,

We would like to thank you for your participation in the RT Prenatal Rapid Test 2018.

This year, 11 colleagues volunteered for diligently and laboriously assessing the submitted reports. We would like to thank you again for your commitment:

Herr MSc. Nijas Aliu (Bern), Frau Prof. Dr. Iris Bartels (Göttingen), Frau Dr. Patricia Emmerich (Baden-Baden), Frau Dr. rer. nat. Katrin Fröbuis (Marburg), Frau Dr. rer. nat. Birgitta Gläser (Freiburg), Frau Dipl.-Biol. Anja Kron (Ingelheim), Frau Dr. rer. nat. Anja Louis (Mannheim), Frau Dipl.-Biol. Anne Pleyers (Salzburg), Frau Dipl.-Biol. Martina Reichert (Würzburg), Frau Dipl.-Biol. Sonja Schweinsberg (Chemnitz), and Frau Dr. Barbara Seipel (Ingelheim).

On 09/10/2018 fixated (alcohol/glacial acetic acid), cultivated amniotic fluid cells and/or DNA from an amniocentesis were shipped for analysis. The cells were from a sonographic abnormal fetus (23th week of gestation). Reason for the amniocentesis was an abnormal ultrasound and suspicion of trisomy 18. It was your task to conduct a routine analysis of the material using a prenatal rapid test (chromosomes X, Y, 13, 18, and 21) and to summarise and upload a diagnostic finding report and a cor-

**Berufsverband Deutscher
Humangenetiker (BVDH) e.V.**

Expanded Committee for Quality Assurance

Members elected:
Prof. Dr. rer. nat. Jürgen Kunz (chairman)
Dipl.-Biol. Susanne Anders
PD Dr. rer. nat. Barbara Fritz
PD Dr. rer. nat./med. habil. Thomas Liehr
Dr. rer. nat. Anja Weise

RT supervisors:
Dr. rer. nat. Sebastian Eck
Dr. rer. nat. Eveline Fiedler
Prof. Dr. med. Claudia Haferlach
Sarah Matos Meder, M. Sc.
Prof. Dr. med. Harald Rieder
Dr. med. Dieter Schäfer

29. April 2019

Coordination Office Quality Assurance

c/o Die Tastatur – Susanne Brandt &
Rainer Göbbels GbR
Feldstr. 30
52249 Eschweiler
Germany

Tel. +49 2403 83 80 54
Fax +49 2403 83 80 56

brandt@bvdh.de
www.bvdh-ringversuche.de

RT-Supervisors Prenatal Rapid Test

Sarah Matos Meder, M.Sc.
Institut für Klinische Genetik und
Tumorzytogenetik Bonn
Maximilianstr. 28 d
53111 Bonn, Germany

Tel. +49 208 96 96 86 70
matos@genetik-bonn.de

Dr. rer. nat. Marion Krüger (deputy)
MCL Medizinische Laboratorien
Freiburgstrasse 634
3172 Niederwangen, Switzerland

Tel. +41 31 328 78 45
marion.krueger@mcl.ch

Administration Office

Liniestraße 127
10115 Berlin, Germany

Tel. +49 30 55 95 44 11
Fax +49 30 55 95 44 14

info@bvdh.de
www.bvdh.de

Bank Details

Deutsche Apotheker- und Ärztebank eG
IBAN DE48 3006 0601 0003 5869 36
BIC DAAEEDDD

USt.-IdNr.: DE 238 391 914
St.Nr. 27/620/53950

VR 28407 B Amtsgericht Charlottenburg

responding laboratory report to the BVDH website. For further documentation, there was an option to upload up to two images. Assessment was based on the submitted diagnostic finding reports.

This year we gave a 2nd case with an ISCN formula and three questions to be answered by you.

In total, 71 laboratories participated in this year's Ring Trial Prenatal Rapid Test, six of which from Switzerland, three from Austria and each one from Poland and Rumania.

Like last year, there were a maximum number of 20 points for Case 1 (including 2 points for ISCN formula, this year for FISH and QF-PCR): four points were awarded for a correct result in the diagnostic report (male, trisomy 18); 2 points each were awarded for

- a) the interpretation of the results in relation to the task and an assessment of the results with regard to the indication (abnormal ultrasound, suspicion trisomy 18) including a statement on the clinical relevance of diagnostic finding (in this category partial points were awarded),
- b) the child's gender reported in the text, and
- c) turn-around-time (≤ 2 days for the findings report).

1 point each was awarded for mentioning diagnostically normal chromosomes, mentioning the abnormal chromosome, a recommendation for genetic counselling, turn-around-time (3–7 days for the finding report), remarks regarding the limitations of the method and for formalities (name, first name, date of birth, correct address, indication, type of sample). A correct karyotype formula (ISCN 2016) was awarded with two extra points.

The fetus' karyotype was determined to be male with a free trisomy 18 (47,XY,+18), confirming the clinical suspicion and in concordance with the fetal ultrasound abnormalities.

70 from 71 laboratories clearly indicated a trisomy 18 with male gonosomal configuration providing therefore a technically correct diagnostic finding report (1 lab used only a probe for chromosome 18, stated the trisomy 18 correctly but gave no information for the chromosomes 13, 21, X and Y). 2 from 71 labs stated a mosaic for trisomy 18.

31 from 71 labs reached the total of 20 points, the mean in Case 1 is 19.1 points!

This time the evaluation of the results with regard to the indication, the recommendation for genetic counseling and the technical limits of the methods were not problematic. A lot of the labs now provide good remarks on their reports now!

Please take care to put the correct material on your reports (for iFISH: cultivated, fixed amniotic fluid cells; for QF-PCR: DNA extracted from amniotic fluid). We think that in every prenatal report the mentioning of the week of gestation should be mandatory, too.

Problems in the ISCN formulas were: description of the loci (MALT instead of MALT1, DSCR instead of DCSR4). You should check the webpages of the FISH-providers from time to time!

For the formulas for QF-PCR (see ISCN 2016, pages 123–124) there seem to be two possibilities:

rsa(13)x2,(18)x3,(21)x2,(X,Y)x1

rsa(13,21)x2,(18)x3,(X,Y)x1

The first puts the chromosomes in the correct order; the second puts together the ones with the correct number, like the gonosomes are put together.

Both possibilities were given by you in the reports and by the assessors; so we decided to accept both formulas as correct. This matter should be discussed during the next BVDH QA workshop meeting in autumn 2019.

The interpretation and the reference to the clinical indication was done very well this time. We think this improvement is due to the fact that it was an abnormal result, confirming the suspicion (see Requirements regarding the finding, S2-LL molecular cytogenetic laboratory diagnostics item 8.1). The following basic information was expected (example):

“We can therefore confirm a trisomy 18 and your clinical suspicion. It correlates with the ultrasound abnormalities.”

Almost all laboratories reported good hybridization quality and quality of the material provided. According to RiLiBÄK the hybridization efficiency needs to be documented for Interphase-FISH.

For the evaluation of the karyotype formula, the participants were asked to pay attention to the current ISCN (2016). On this basis, the following criteria were taken into account:

Deduction	Error
-1	sequence of contig probes
	simultaneously hybridized probes without brackets
	number of analyzed cells in brackets [xx]
	„cen“, „cep“, „LSI“, „XA“
	clone separation with colon instead of a forward slash
	multiplication sign erroneously inside/outside the brackets
	ISCN not mentioned, not even in the text
-0.5	„small“ mistakes like spaces after nuc ish and before the first bracket
	lack of colons (e.g. between the brackets for the different probe mixes)
	errors in the clone names (e.g. D21S34 instead of D21S342)
	ISCN version not mentioned or ISCN 2013 used

For Case 2 all the participants noticed the trisomy 21. Unfortunately, not all mentioned the male genotype in question number 3 (deduction of 0.5 points).

For the correct FISH formula some mistakes were made again with wrong clone names. Even if you use other probes in your lab you can easily check the correct names on the provider’s webpage (here: Metasystems).

We recognized with your answers that we asked for a karyotype formula instead of an ISCN formula for FISH/QP-PCR. Moreover, we put “(X/Y)x2” in the wrong QF-PCR-formula. So you were not sure if we talked about a “47,XY,+21” or a “49,XXYY,+2”. We accepted therefore both answers and we apologize for the misunderstanding.

40 from 71 labs got the 5 points here, the mean was 3.9 points.

You can find your individual results on the BVDH ring trial platform www.bvdh-ringversuche.de. Please log in and to go “Ring trials – completed”. Look for RT Prenatal Rapid Test 2018 and click on “Assessment” in the respective line.

Any objections against this RT in general or your individual assessment must be sent in text form to the Coordination Office (brandt@bvdh.de) within four weeks after publication of this final report.

Finally, we would like to thank you for your participation and confidence. We would be glad if you could not only contribute as a participant, but also volunteer as an assessor for the ring trial 2019. In case you would like to support us with the assessment, please get in contact with Mrs. Brandt (brandt@bvdh.de, phone: +49 2403 838054). Assessors are welcome to define their workload in advance and will receive a confirmation about their activity and commitment as an assessor.

We are grateful for suggestions and criticism.

Yours sincerely,



Sarah Matos Meder
Ring Trial Supervisor



Dr. Marion Krüger
Deputy RT Supervisor



Prof. Dr. Jürgen Kunz
Chairman of Expanded
Committee for QA