## Methods and diagnostic quality

In the NIPD-RhD, cell-free DNA from the placenta is tested. Using qPCR, the exons 5, 7 and 10 of the RhD gene are amplified and evaluated. If the test result is positive for all three exons, the analyzed sample is classified as RhD-positive. If the test result is positive for only one or two exons, the overall result is evaluated as being not diagnostically conclusive. All test results of the three exons must be negative in order for the overall result of the sample to be classified as RhD-negative.

| Test result | | | Classification |
|---|---|---|---|
| Exon 5 | Exon 7 | Exon 10 | |
| + | + | + | RhD-positive |
| – | – | – | RhD-negative |
| 1 or 2 exons positive | | | not diagnostically conclusive |

## IQWiG: Prenatal test is equivalent to the postnatal test

In its final report (March 2018)[10], the Institute for Quality and Efficiency in Health Care (IQWiG) certifies that the non-invasive prenatal determination of the fetal Rhesus factor has a very high level of sensitivity and specificity. Because of the high level of sensitivity of the test, only very few cases of anti-D prophylaxis which were erroneously not administered antepartum can be expected. In addition, the postnatal tests also yielded false-negative results at rates similar to those of the prenatal tests. The prenatal test is therefore equivalent to the postnatal test.


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2 Hemotherapy guideline, overall amendment 2017, chapter 4.12.1.5
3 237th statement from the German Society of Gynecology and Obstetrics (DGGG). Nichtinvasive Bestimmung des fetalen Rhesusfaktors zur Vermeidung einer mütterlichen Rhesus-Sensibilisierung im Rahmen der Vorsorgeuntersuchung gemäß Mutterschafts-Richtlinien (Mu-RL) [Non-invasive determination of the fetal Rhesus factor to avoid maternal Rhesus sensitization during screening in accordance with the maternity directive (Mu-RL)]. www.dggg.de/leitlinien-stellungnahmen/stellungnahmen/nichtinvasive-bestimmung-des-fetalen-rhesusfaktors-413, accessed on 01/21/2019.
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7 Instruction manual: Jaques Boy Biotechnology Institute. Free DNA Fetal KitR RhD. Noninvasive fetal RHD genotyping from free fetal DNA in maternal RhD-Negative pregnant women blood (Real-Time PCR). Product identification: 502080233. Manual version 16/03/2018.
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10 IQWiG report no. 607. Nichtinvasive Bestimmung des fetalen Rhesusfaktors zur Vermeidung einer mütterlichen Rhesussensibilisierung [Non-invasive determination of the fetal Rhesus factor to avoid maternal Rhesus sensitization]. Order D16-01. Final report, version 1.0., www.iqwig.de/download/D16-01_Bestimmung fetaler-Rhesusfaktor_Abschlussbericht_V1-0.pdf. Status: 03/20/2018, accessed on 08/14/2018.


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# NIPD-RhD

Non-invasive prenatal RhD genotyping

lifecodexx Information for physicians

03

# NIPD-RhD – The Rhesus test from Eurofins LifeCodexx

**Anti-D prophylaxis often unnecessary**
In general, anti-D prophylaxis is recommended to RhD-negative pregnant women in the 28th week of pregnancy, regardless of whether their unborn child or the child's father is RhD-positive. However, the prophylaxis is unnecessary in about 40% of the RhD-negative women since their unborn children are also RhD-negative.[1]

**Non-invasive prenatal RhD determination from maternal blood**
Now you have the option of determining the fetal Rhesus factor non-invasively from the blood of the RhD-negative mother (NIPD-RhD), with a high level of diagnostic reliability. As a result, you can decide whether anti-D prophylaxis is indicated in order to use it specifically only for those RhD-negative pregnant women who are actually expecting an RhD-positive child.

Anti-D prophylaxis in pregnant women is not necessary if the fetus was determined to be RhD-negative using a validated method. After delivery, the RhD characteristic is to be determined, preferably from umbilical cord blood.

Hemotherapy guideline, overall amendment 2017[2]

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# Benefits and use

**Benefits of the NIPD-RhD**
According to the German Society of Gynecology and Obstetrics (DGGG), you avoid the following adverse effects in those pregnant women in whom prophylaxis is not indicated[3]:

- Potential infection through the transmission of pathogens with the administration of the anti-D prophylaxis (human immunoglobulin)
- Allergoid/anaphylactic reactions
- Shortened inpatient hospitalization for RhD-negative mothers since they can receive anti-D prophylaxis immediately after delivery if the test result is positive
- The anti-D immunoglobulin is currently obtained from immunized donors and imported

**Limits of the test**

- False-positive test results are possible in the case of a rare genotype, non-functional RhD variant[1] or a bone marrow donation[4]
- A test result cannot be reported if the mother is a carrier of the RhD gene
- False-negative results are also fundamentally possible[5,6]

# NIPD-RhD Rhesus test

| 95,1%[7] | 100%[7] |
|---|---|
| Specificity | Sensitivity |

- Non-invasive prenatal RhD genotyping from maternal blood
- For RhD-negative pregnant women with singleton pregnancy
- Between gestational weeks 11 + 0 and 25 + 0 (recommended)
- CE-marked IVD[7,8,9] – reimbursed in France
- Test performed by Eurofins Biomnis, France
- Delivery time 10 working days per analysis (Monday to Friday, without public holidays)

**Exemplary diagnostic strategy for RhD-negative pregnant women**

**Non-immunised patient**

**Blood sampling & express delivery** (responsible doctor)

**Test result** (generally 10 working days)

**RhD-positive** or **inconclusive*** → **Anti-D prophylaxis is indicated**

**RhD-negative** → **Repeat analysis** 2 weeks later & after week 18 + 0

- **RhD-positive** or **inconclusive*** → **Anti-D prophylaxis is indicated**
- **RhD-negative** → **Anti-D prophylaxis is not indicated**

**Timeframe for blood sampling**
We recommend blood sampling latest in gestational week 25 + 0. This will ensure a test result latest in gestational week 29 – including a repetition, if necessary.

**Immunised patient**

**Blood sampling & express delivery** (responsible doctor)

**Test result** (generally 10 working days)

**RhD-positive** or **inconclusive*** → **Specific monitoring**

**RhD-negative** → **Repeat analysis** 2 weeks later & after week 18 + 0

- **RhD-positive** or **inconclusive*** → **Specific monitoring**
- **RhD-negative** → **Standard monitoring & relief of the patient**

**Repeat analysis to confirm a negative test result**

- You will receive a special blood collection set for the repeat analysis.
- Fill both blood tubes
- Tick „repeat blood sample (if 1st analysis failed)" on the form
- Send both blood samples together with the completed form

* due to biological limitations