NeoPrediX B.1

Operating Instructions EN

The following operating instructions refer to software version:

V1.2.2/CE

CE 0297

Contents

1. Symbols and abbreviations

1.1. Symbols for labeling

Symbol	Meaning
	Manufacturer
	Distributor
	Shows the date on which the medical device was manufactured.
MD	Medical device
REF	Product name
LOT	Software version
CE 0297	CE conformity marking and identification number of the notified body involved in the conformity assessment procedure
www.NeoPrediX.com	Please refer to the electronic instructions for use (PDF). Download: www.neopredix.com
i	Information
▶	Action prompt, work step
UDI	One-time product identification

Table 1: Symbols for labeling

1.2. Symbols used in the software

Symbol	Meaning
👁	Optical measurement / non-invasive / transcutaneous bilirubin value / TcB
💧	Total serum bilirubin / TSB
📈	Nomogram Curve Show/Hide
⌀	Prediction Show/Hide
⊗	Marker for TcB
⊗	Marker for TSB
✕	Marker for TcB
✕	Marker for TSB
PDF	PDF
⊕	Add
✓	Confirm
⊗	Cancel
⊕	Add
📅	Calendar
✎	Edit
🗑	Delete

Symbol	Meaning
❗	Mandatory condition not met
ℹ	Information / Informal note
⚠	Warning

Table 2: Symbols used in the software

2. Definitions of terms and abbreviations used

2.1. Definitions of terms

This section defines basic terms that will be used below.

Term	Explanation
Bilirubin measurement	Includes: • Day of measurement indicated by the date • Time of measurement indicated by the time (clinic time zone) • Bilirubin value • Unit of measurement • Type of measurement
Bilirubin progression	Dynamic progression of bilirubin values over a specified period of time
Patient / Newborn	Equivalent terms used in the document. For better readability, the generic masculine form is used, but it refers to both female and male patients.

Table 3: Definition of terms

2.2. Abbreviations used

Abbreviation	Explanation
TcB	Transcutaneous bilirubin value
TSB	Total serum bilirubin
AAP 2022 Guidelines	American Academy of Pediatrics (2022) "*Clinical Practice Guideline Revision: Management of Hyperbilirubinemia in the Newborn Infant 35 or More Weeks of Gestation*"

Table 4: Abbreviations used

3. Intended use

NeoPrediX B.1 is a software to predict bilirubin progression in neonates.

NeoPrediX B.1 can predict bilirubin progression in the first week of life up to 60 hours after the last measurement. Bilirubin (in µmol/l or mg/dl) is represented as a graph in a diagram depending on postnatal age (in hours).

3.1. Indication

NeoPrediX B.1 supports the indication of "screening for and/or prevention of hyperbilirubinemia" in newborns with a gestational age ≥ 34 weeks.

3.2. Contraindication

The following general risk factors are contraindicated:

- Phototherapy before the first bilirubin measurement
- Neonatal cholestasis (congenital or acquired liver dysfunction of various causes during the neonatal period)
- Hydrops fetalis (congenital severe anemia due to Rh or blood group incompatibility, infections, or cardiovascular malformations)
- Neonatal sepsis
- Severe asphyxia (Apgar1 Score < 4)
- Hypoxic ischemic encephalopathy
- Malformations of the digestive tract and/or the liver
- Systemic antibiotic treatment
- Congenital metabolic diseases

3.3. User

NeoPrediX B.1 is intended for use exclusively by medical professionals (users).

4. Safety information

4.1. Safety notice classification

The safety instructions and important usage instructions in this document are classified based on risk.

► Familiarize yourself with the meanings of the classifications before using the software.

NOTE!
Indicates a potentially harmful situation.
If it is not avoided, it can lead to loss or compromise of data.

4.2. Safe use

To use NeoPrediX B.1 safely, please follow the operating instructions below:

► Read these operating instructions and keep them for future reference.

i	The operating instructions are also permanently integrated into NeoPrediX B.1 and can be accessed at any time.
i	If you need a replacement for the user manual, please contact NeoPrediX AG through the help function in the tool or through the contact information (see section 10). We will send you a copy as soon as possible.

► Use NeoPrediX B.1 exclusively according to its intended use (see section 3).
► The user is responsible for the proper entry of data and values.
► Perform the functional test according to section 7 to verify the correct operation of NeoPrediX B.1.

4.3. Foreseeable misuse

NOTE!
Use of the results for therapy decision-making ► Do not use the results of NeoPrediX B.1 for therapy decision-making.

4.4. General warnings

4.4.1. Incidents

► Report any incidents to the relevant authority **and** to NeoPrediX AG in accordance with the regulations applicable in your country.

► To report to NeoPrediX AG, use the form in the software's help function.

4.4.2. Malfunctions

► Report any malfunctions to NeoPrediX AG.

► Use the form in the software's help function.

5. Specifications and Operation

5.1. Minimum technical requirements

To use NeoPrediX B.1, you will need a device with the following characteristics:

- PC with input devices or tablet PC
- Internet connection (DSL with 1 Mbit/s or better)
- Up-to-date browser (Google Chrome, Microsoft Edge, Mozilla Firefox), not more than 6 months old
- Processor: 1 GHz or higher
- RAM: 1 GB or more
- Monitor resolution depends on scaling: At least 1376 x 786 pixels or higher

5.2. Minimum medical requirements

To enable a prediction of bilirubin progression, the following patient medical parameters must be input into NeoPrediX B.1:

Data required	Acceptance criteria for the specified values
Date of birth	---
Time of birth	---
Gestational age in weeks and days	34+0 to 42+6
Weight at birth	1500 to 5000 g
For a gestational age ≤ 36+6	1500 g (minimum)
For a gestational age ≥ 37+0	2500 g (minimum)
Delivery mode	Vaginal or cesarean
Measured TSB or TcB values	One or more measured value(s)
Data in mg/dl	1 - 18
Data in µmol/l	17.1 - 307.8

Table 5: Minimum requirements and acceptance criteria for data to predict bilirubin progression

> **Limits for prediction**
> A prediction cannot be made if the specified values are outside the stated acceptance criteria.
> Please also consider the bilirubin limits based on postnatal age as outlined in section 6.6.1.

5.3. Computer model used to predict bilirubin progression

The algorithm used in NeoPrediX B.1 is based on a mathematical computer model that predicts the progression of bilirubin as a function of postnatal age. This model consists of a differential equation with medically and physiologically motivated components that reflect the production and elimination of bilirubin in the body.

In healthy individuals, the production and elimination of bilirubin are in balance, resulting in constant bilirubin values. In premature or full-term infants, production may be increased and elimination may be reduced in the first few days of life. This leads to increased bilirubin values in the first few days of life. After reaching the peak of bilirubin progression, production and elimination gradually return to a healthy balance. This leads to a subsequent decrease until bilirubin is normalized.

The bilirubin progression for a newborn is predicted based on one or more bilirubin measurements, as well as individual medical parameters of the newborn such as gestational age, birth weight, and delivery mode. In the algorithm, the mathematical model is calibrated using a statistical method (Bayesian estimation) based on the individual input. As a result, each newborn obtains its individual adjustment.

Details about the mathematical computer model can be found in patent „EP 3688473 B1" or "US 11,656,234 B2".

6. Using NeoPrediX B.1

NOTE!

Data compromise

Access to the system by unauthorized persons can lead to data loss or manipulated patient data and system settings

► If you have received your personal information, change the initial password to a personal password after logging in for the first time.

► Make sure that your personal password is known only to you.
Change your password immediately if it could have become known to another person.

► Use a sufficiently complex password that cannot be easily guessed.

► Enter your personal password manually each time you log in, without saving it in the browser.

► Log out of NeoPrediX B.1 when you are no longer using NeoPrediX B.1.

6.1. Signing in to NeoPrediX B.1 without a connection to the hospital information system

► Sign in with your personal information to use NeoPrediX B.1.

The necessary information in the login dialog are:

- Client name of your facility
- Your personal username
- Your personal password

NeoPrediX will give you the initial login information.

6.1.1. Changing the password

▶ Log in to NeoPrediX B.1 with your personal information if you want to change the password.

▶ Select the "Change Password" function using the arrow symbol next to your username.

Figure 1: Password manager

▶ Enter your current password.

▶ Enter a new password that meets the specified minimum requirements.

▶ Re-enter your new password for security purposes.

6.1.2. Password recovery

If you forget your personal password, you can assign a new password.

▶ Open the login dialog.
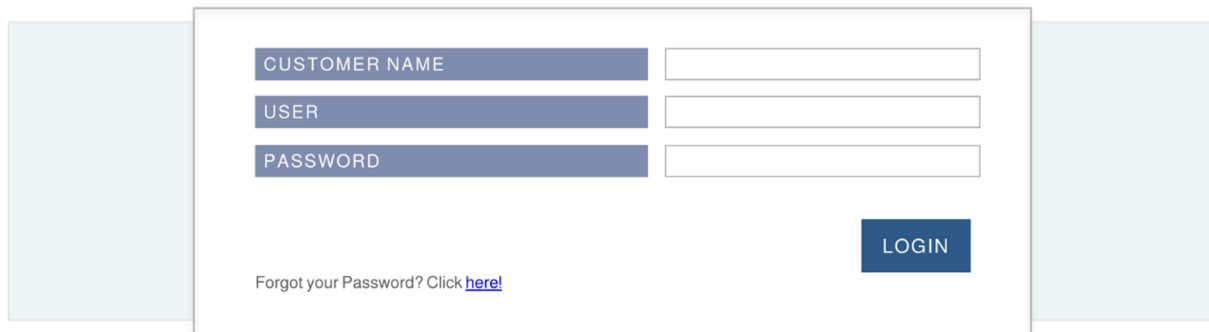
Figure 2: Login dialog

▶ Click on the link "here".

▶ Enter your client name.

▶ Enter your username.

▶ Submit the request.

An email will be sent to the email address associated with the user.

▶ Check the inbox of the associated email account.

▶ Follow the instructions in the email to reset your password.

6.2. Signing in to NeoPrediX B.1 with a connection to the hospital information system

If NeoPrediX B.1 is connected to your hospital information system and authentication is enabled through your hospital information system:

► Enter the client name of your facility in NeoPrediX B.1.

You will be redirected to your authentication provider. After successful authentication, you will be redirected back to NeoPrediX B.1.

6.3. Logging out of NeoPrediX B.1

To log out from NeoPrediX B.1:

► Select the "Logout" function using the arrow symbol next to your username.
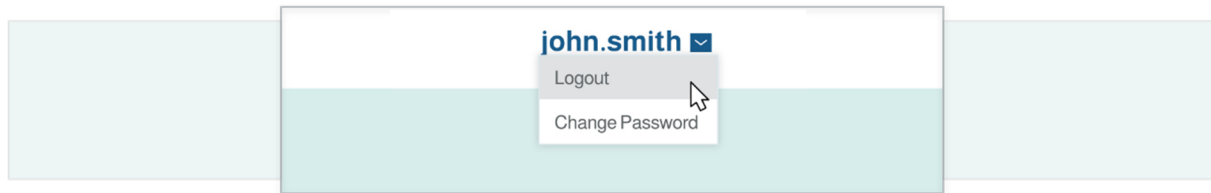
Figure 3: User logout

6.4. Viewing patient data

After logging in, you will find yourself in the patient overview, also known as the "Dashboard".

The patient overview shows the patients of your facility stored in NeoPrediX B.1. By default, patients who were born within the last 30 days will be shown. You can set this value during installation or afterwards. Please contact our customer support for assistance with this.

The patient overview can be accessed at any time by clicking on "Dashboard" at the top of the screen.
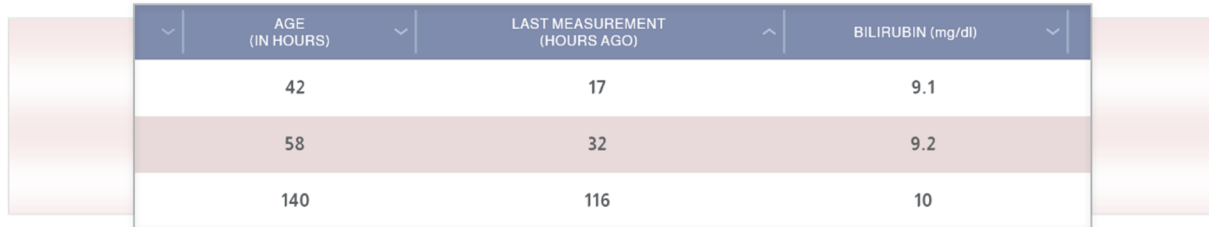
The following information is shown for each patient:

- Patient ID
- Patient name
- Date and time of birth
- Age (in hours)
- Hours elapsed since the last bilirubin measurement
- Bilirubin value at last measurement

By default, the patient overview is sorted by the time of birth, with the youngest patients shown first.

6.4.1. Adjusting the sorting order in patient overview

▶ By clicking on the arrow symbol, select the column according to which you want to sort the entries.

▶ To reverse the sorting direction, click again on the arrow symbol in the column.

AGE (IN HOURS)	LAST MEASUREMENT (HOURS AGO)	BILIRUBIN (mg/dl)
42	17	9.1
58	32	9.2
140	116	10

Figure 4: Excerpt from the patient overview table

6.4.2. Finding patients
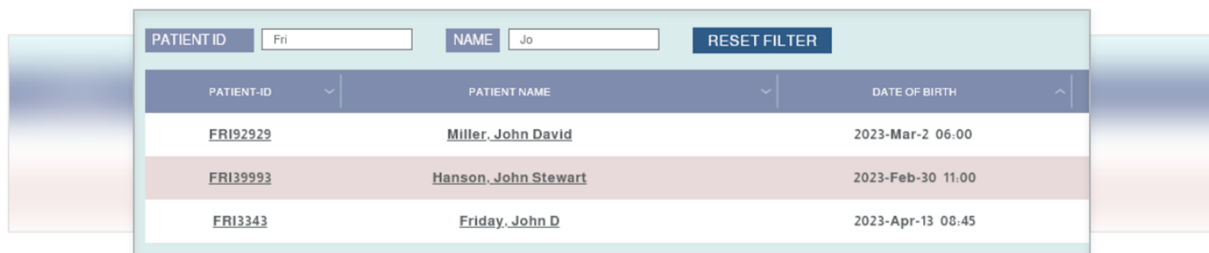
Patients are searched based on the patient ID or the patient's name.

▶ Enter the patient ID, name, or parts of it into the respective search field of the patient overview (see Figure 5).

After each input, only the patients that match this input data will be shown.

To show all patients again, reset all the filters.

▶ Select "RESET FILTER" to delete all entered filter criteria.

PATIENT ID	Fri	NAME	Jo	RESET FILTER

PATIENT-ID	PATIENT NAME	DATE OF BIRTH
FRI92929	Miller, John David	2023-Mar-2 06:00
FRI39993	Hanson, John Stewart	2023-Feb-30 11:00
FRI3343	Friday, John D	2023-Apr-13 08:45

Figure 5: Patient filter

6.4.3. View patient information

Accessing the detailed information of an individual patient:

▶ Click on the respective patient ID or the patient's name.

The patient information page is divided into 3 sections:

- Patient data
- Measurement data
- Diagram area with various options

On the patient information page, you have the following options:

- Add, adjust, or delete bilirubin value(s) (*) [see section 6.6]
- Adjust patient data (*) [see section 6.5]
- Delete patient data completely from the system [see section 6.5.5]
- Create final report [see section 6.9]
- Show Bhutani nomogram [see section 6.8]
- Show prediction of bilirubin progression [see section 6.7]
- Show phototherapy thresholds [see section 6.8]
- Show zones of discharge recommendations [see section 6.8]
- Show bilirubin rate of increase [see section 6.8]

For detailed information, please refer to the referenced sections.

> (*)
> Bilirubin values and patient data can be changed only if there is no connection to the hospital information system.

6.5. Entering and editing patient data

6.5.1. Adding new patients

To add new patients:

▶ Select the "ADD NEW PATIENT" button in the patient overview (Dashboard).
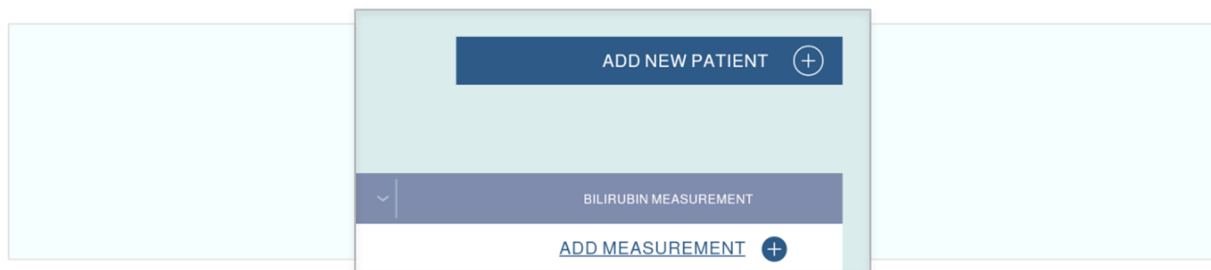
Figure 6: Adding a new patient

The input mask for patient data appears.

6.5.2. Entering patient data without a connection to the hospital information system

The following information is mandatory to enable a prediction for bilirubin progression:

- Patient ID
- Date and time of birth
- Gestational age on day of birth
- Weight at birth
- Delivery mode (vaginal or cesarean)
- Risk factors (yes/no; according to AAP 2022 Guidelines)

► Enter the **Patient ID** in the input mask that appears

The **Patient ID** must meet the following conditions:

- Unique for each patient
- Length between 1 and 50 characters
- No special or control characters ".", "\", or Unicode characters U+007F - U+009F
- Allowed special characters are, for example:

Character	Description		Character	Description
;	Semicolon		@	At sign
,	Comma		&	And
/	Slash		=	Equals sign
?	Question mark		+	Plus
:	Colon		$	Dollar

Table 6: Allowed special characters for the patient ID

► Enter the **date of birth** using one of these options:
- Choose the date directly from the past days, OR
- Enter the date in the format "yyyy-mm-dd" OR
- Select the date using the calendar tool

► Enter the **time of birth** in 24-hour format "hh:mm".

► Select the **gestational age** in weeks and days.

► Enter the **weight at birth** in grams.

► In the **Risk Factors** field, click "yes" if at least one of the following neurotoxic risk factors for hyperbilirubinemia is evident, according to the AAP 2022 Guidelines:

- Gestational age < 38 weeks (the earlier the birth, the greater the risk)
- Albumin < 3.0 g/dl
- Isoimmune hemolytic diseases (including positive direct antiglobulin test), G6PD deficiency, or other hemolytic diseases
- Sepsis
- Significant clinical instability in the past 24 h

OTHERWISE click "no".

► Enter the patient name in the **name fields** (last name, first name, and middle name). You can enter up to 50 characters each, optionally. Numbers are not allowed.

> ℹ   You can identify missing or invalid information by a red border.

► Click "CONFIRM" after entering all known information.
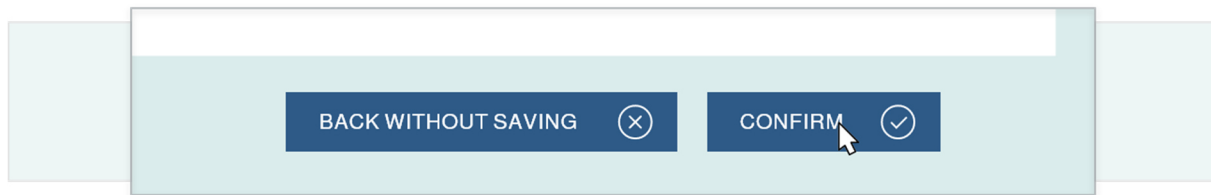
Figure 7: Confirming patient data

► Check the information shown for accuracy.
► Confirm the entries by clicking "SAVE".

> ℹ   You can make changes by clicking "BACK WITHOUT SAVING" and going back to the input screen.

6.5.3. Entering patient data with a connection to the hospital information system

When NeoPrediX B.1 is connected to your hospital information system, you can import patient data. These patient data will be updated with every access through the hospital information system.

To import data on a patient:

▶ Enter the "Medical Record Number (MRN)".

▶ Select "Load patient".

The patient data fields are automatically filled with the data from the hospital information system.

▶ Click "CONFIRM" (see Figure 7).

▶ Check the information shown for accuracy.

▶ Confirm the entries with "Save".

> **ℹ** You can make changes by clicking "BACK WITHOUT SAVING" and going back to the input screen.

6.5.4. Editing patient data

NOTE!
Data loss
▶ Save entered data and values before closing the software.

If there is no connection to a hospital information system, you can edit the data of existing patients.

▶ Open the patient information on the respective patient.

▶ Select the "EDIT PATIENT DATA" function.
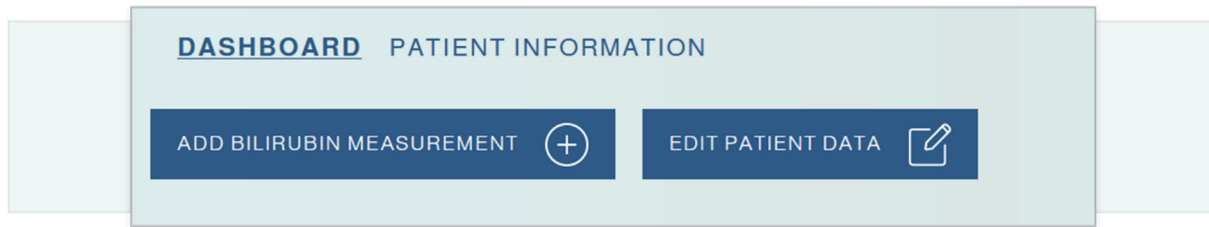
Figure 8: Patient Information Dashboard

▶ Edit the patient data in the input mask, if necessary. The same conditions apply as when adding a new patient.

> ℹ️ You can change the date and time of birth only if the bilirubin value has not been entered for this patient.

▶ After all adjustments are made, select "Confirm" to accept the changes.

> ℹ️ If you adjust patient data that have an impact on the prediction of bilirubin progression, you will be warned with a corresponding message.
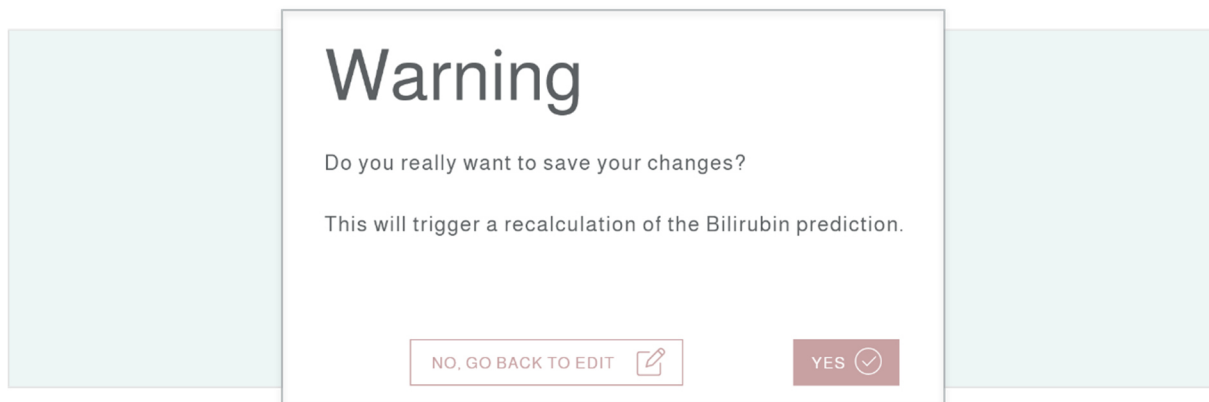
Figure 9: "Changed Data" Warning

▶ Check to make sure the changes are correct.

New information is shown in the respective field, with the previous content shown in addition next to or below the corresponding field.

Figure 10: Comparison of changed data

► Confirm the adjustments by selecting "Save" if all the information is correct.

ℹ️ You can make changes by clicking "BACK WITHOUT SAVING" and going back to the input screen.

6.5.5. Deleting patient data

To delete patient data from the system:

► Select the "recycle bin" symbol.
► Confirm deletion if you are certain that the patient's record should be deleted.

6.6. Adding and editing bilirubin measurements

6.6.1. Adding a bilirubin measurement

NOTE!
Using the browser's autofill function
Automatically filled fields may contain incorrect entries for the patient. This can lead to an **anomalous prediction.**
▶ Do NOT use the browser's automatic fill functions ("autocomplete" or "autofill") when entering measurement values!

NOTE!
Data loss
▶ Save entered data and values before closing the software.

If there is no connection to the hospital information system, there are two options to add a bilirubin measurement for a patient.

▶ Select the "Add Measurement" function in the patient overview for the corresponding patient, OR

Figure 11: Excerpt from the patient overview

▶ Select "ADD BILIRUBIN MEASUREMENT" in the patient information (Dashboard) of the corresponding patient.
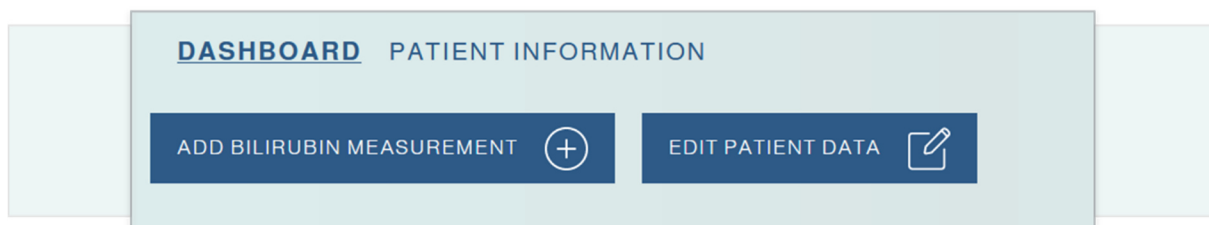
Figure 12: Excerpt from the Dashboard
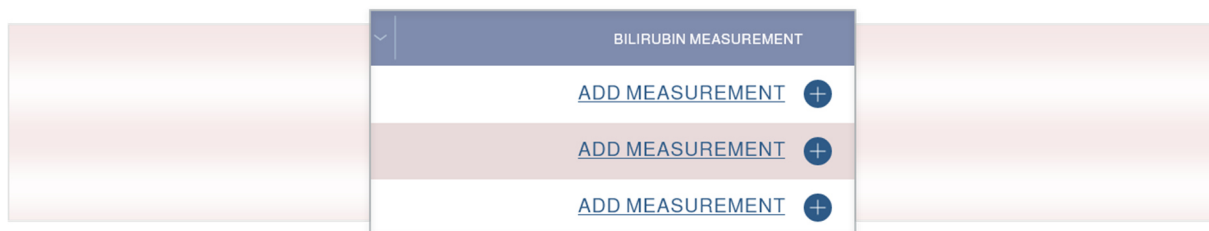
► Check the patient data shown next to the input mask for the bilirubin value.

► Enter the time of measurement.

► Enter the measured bilirubin value.

- in mg/dl or µmol/l, as desired
- rounded to one decimal point
- required minimum value: 1.0 mg/dl or 17.1 µmol/l

► Select the type of measurement being performed, TSB or TcB.

The maximum value to obtain a prediction of bilirubin progression depends on the postnatal age of the patient.

Postnatal age in hours	Maximum bilirubin value	
	mg/dl	µmol/l
between ≥ 8 and ≤ 60	15.0	256.5
between > 60 and ≤ 72	16.0	273.6
between > 72 and ≤ 84	17.0	290.7
between > 84 and ≤ 120	18.0	307.8

Table 7: Maximum permissible bilirubin values depending on postnatal age

i	Measurement values higher than the maximum values can also be entered; however, in that case, the bilirubin progression cannot be predicted.
i	You can identify missing or invalid information by a red border. After entering all the data, proceed to the confirmation.

► Check the information shown for accuracy.

► Confirm the entries by selecting "Save".

i	You can make changes by clicking "BACK WITHOUT SAVING" and going back to the input screen.
i	If there is a connection to the hospital information system, the bilirubin measurements will be automatically imported into the system when the patient is added and will be updated every time the patient is accessed. New bilirubin measurements will be automatically inserted and old possibly incorrect ones will be updated or removed.

6.6.2. Editing an existing bilirubin measurement

NOTE!

Using the browser's autofill function

Automatically filled fields may contain incorrect entries for the patient. This can lead to an **anomalous prediction.**

> ▶ Do NOT use the browser's automatic fill functions ("autocomplete" or "autofill") when entering measurement values!
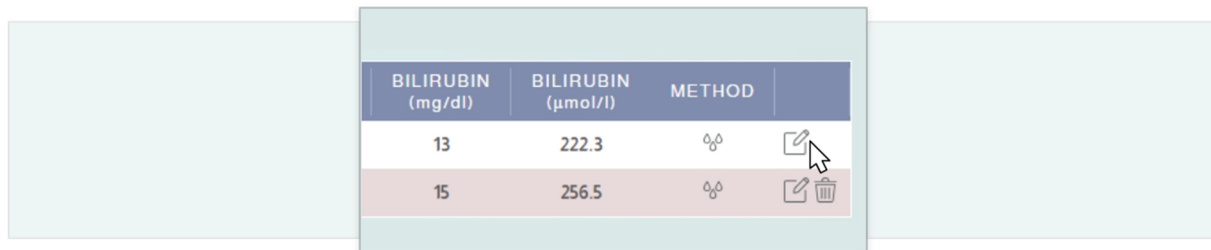
NOTE!

Data loss

> ▶ Save entered data and values before closing the software.

If there is no connection to the hospital information system, you can edit already entered bilirubin measurements for a patient.

> ▶ Open the patient information (Dashboard) of the respective patient.
> ▶ Click on the parameter to be changed in the measurement table.
> - time,
> - date, OR
> - measurement using the associated "Edit" icon

Figure 13: Excerpt from the patient's Dashboard

> ℹ You can edit the measurement information in the input mask. The same conditions apply as when entering a new bilirubin measurement.

► Enter the changes.

► Continue to the confirmation.

► Check the changes shown for accuracy.

> ℹ️ New information is shown in bold, with the previous content shown in addition next to or below the corresponding field.

► Confirm the changes by selecting "Save" if all the information is correct.

> ℹ️ You can make additional changes by going back to the input screen.

> ℹ️ If there is a connection to the hospital information system, the bilirubin measurements will be automatically imported into the system when the patient is added and will be updated every time the patient is accessed. New bilirubin measurements will be automatically inserted and old possibly incorrect ones will be updated or removed.

6.7. Prediction of bilirubin progression

> **i** Detailed explanations on how to determine the maximum prediction period for bilirubin progression can be found in Appendix I.

6.7.1. Input rules for bilirubin measurements

There are three input rules regarding bilirubin measurements to obtain a prediction of bilirubin progression.

Rule 1: Prediction period with a maximum length of 30 hours

If a TSB measurement is available between 8 and 72 hours after birth, a maximum prediction of 30 hours after the last measurement is possible.

Rule 2: Prediction period with a maximum length of 48 hours

If any measurement is taken between 8 and 72 hours after birth, and another measurement is taken between 24 and 120 hours after birth, with an interval of at least 8 hours, a maximum prediction of 48 hours after the last measurement is possible. There is an exception for two TSB measurements; see the following rule 3.

Rule 3: Prediction period with a maximum length of 60 hours

If a TSB measurement is taken between 8 and 72 hours after birth, and another TSB measurement is taken between 24 and 120 hours after birth, with an interval of at least 8 hours, a maximum prediction of 60 hours after the last measurement is possible.

The input rules 1 - 3 are visualized in the following Figure 14.

Bilirubin measurements (postnatal age)		Maximum prediction period
8 h ----➤ 72 h 🔴		30 h
8 h ----➤ 72 h ⊕ 24 h ----➤ 120 h 👁		48 h
8 h ----➤ 72 h 👁 ⊕ 👁 or 🔴 24 h ----➤ 120 h		
8 h ----➤ 72 h 🔴 ⊕ 24 h ----➤ 120 h 🔴		60 h
◄----➤ Interval of at least 8 h		TSB: 🔴 TcB: 👁

Figure 14: Summary of the three input rules

6.7.2. Invalid bilirubin measurements

Bilirubin measurements that fall below or exceed the defined limits (see section 6.6.1), are shown in gray. Once at least one bilirubin measurement has been marked as invalid, the bilirubin progression can no longer be predicted.

6.7.3. Display prediction of bilirubin progression

Prediction of a patient's bilirubin progression can be displayed as follow.

▶ Open the patient information on the respective patient. The diagram shows the bilirubin values already recorded.

▶ Select "Show prediction" below the chart.

> **i** If this option is not available, the recorded bilirubin values do not allow for prediction (see section 6.7.2).
>
> ▶ Check if you can meet the requirements by taking another measurement.

If the requirements are met, NeoPrediX B.1 provides a prediction of bilirubin progression up to:

• a maximum of 60 hours after the last measurement (depending on the number and type of measurements), see Appendix I and

• a maximum of 144 hours after birth

> **i** The predictive accuracy of bilirubin progression may vary due to individual changes (e.g., biological factors) or measurement errors in the laboratory.
>
> ▶ Only use bilirubin measuring devices with CE and/or FDA approval for bilirubin measurement that have a maximum measurement accuracy of +/- 7%.

The prediction of bilirubin progression (in mg/dl and µmol/l) is shown as a graph in the diagram depending on postnatal age (in hours). TSB measurements are represented in the diagram with a red cross, and TcB measurements are represented with a blue cross. The following information is shown:

① Prediction of bilirubin progression based on previous measurements (in the example, two red crosses)

② Start of prediction from the last measurement and start of the clinically relevant safety range, indicated by a vertical line at +10%

③ End of the prediction period and end of the clinically relevant safety range, indicated by a vertical line at +25%

④ Upper limit of the clinically relevant safety range over the prediction period, increasing from +10% to +25%

⑤ Clinically relevant safety range represented as an area over the prediction period

⑥ Prediction range given by the two predicted bilirubin values from +0% to +25% at the end of the prediction period

Figure 15: Example of prediction chart

6.8. Nomograms based on Bhutani and AAP 2022 guidelines, and additional information

Different nomograms and additional information based on the AAP 2022 guidelines can be shown in NeoPrediX B.1.

▶ Select "Show Nomogram Curves" to show the Bhutani nomogram.

▶ Select "Show AAP 22 Phototherapy Threshold" to show the phototherapy thresholds based on gestational age and the indicator for existing hyperbilirubinemia neurotoxic risk factors according to the AAP 2022 guidelines (see ① in Figure 16).

▶ Choose "Show AAP 22 Risk Nomogram Zones" to show the different zones of discharge recommendations according to the AAP 2022 guidelines (see ② in Figure 16).
  • The bilirubin increase rate is shown, see ③ in Figure 16.
  • The difference from the phototherapy threshold based on the last bilirubin measurement is shown; see ④ in Figure 16.

Figure 16: Example of AAP guidelines
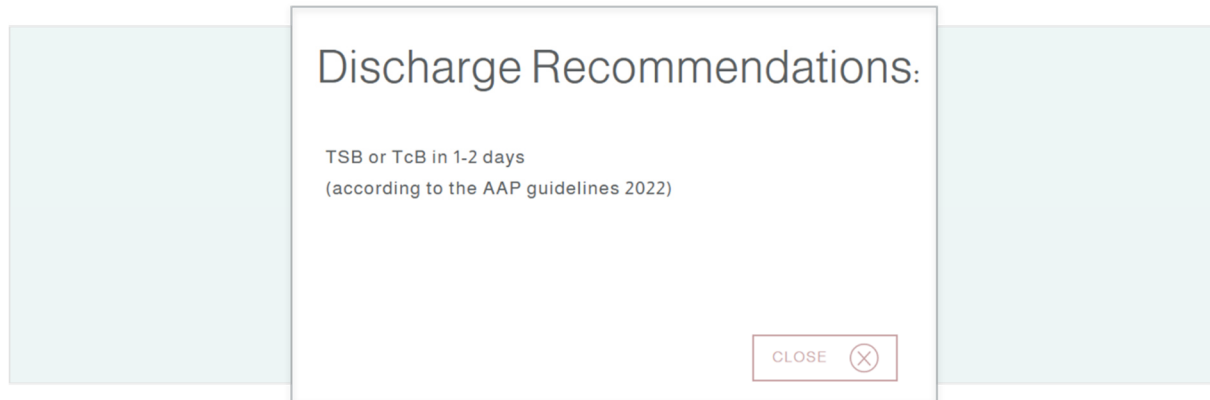
Figure 17: Example of recommended measures related to patient discharge

6.9. Generating a final report

You can generate a final report with the following content:

- the patient information
- all bilirubin measurements recorded
- the predicted bilirubin progression

▶ Select the "Final Report" function in the patient information (Dashboard) of the respective patient.

The report will be shown as a PDF file in a new browser window. From there, you can download or print the report.

6.10. Warnings for measurements

As soon as a test criterion for a measured value is over or under the limits, a warning will be shown in the form of a warning symbol.

► Click on the warning symbol shown to see more details.

The individual details of the test criteria will now be explained in more detail.

Test criterion for minimum and maximum weight values
The permissible measurement values depend on the postnatal age of the measurement. Please refer to section 6.6.1.

Test criterion for minimum and maximum measurement time points
The allowable postnatal age range at the time of the measurements is 1 to 120 hours. If the results are outside of this range, the bilirubin measurement will be marked as invalid and no further bilirubin results can be shown. Furthermore, a warning message will be shown.

Plausibility check of consecutive bilirubin measurements
If two consecutive bilirubin measurements have the same value, a warning will be generated and the measurement value to be compared will be shown next to the last measurement.

Test criterion: rate of increase
The rate of increase between the measurements is calculated.
The prediction of bilirubin progression depends on postnatal age and the determined rate of increase. If the results fall over or under the limits for the rate of increase, no prediction will be made. A warning message displays if the limits for the rate of increase are exceeded.

Postnatal age of the patient	Rate of increase in mg/dl/h	Effect
1 - 120 hours	**≥ 1.5** or **≤ -1.5**	• No prediction of bilirubin progression possible • Any later measurement will be shown in gray (invalid) on the diagram • Warning in the table
24 - 120 hours	**≥ 0.2** mg/dl/h	• Warning in the table
1 - 24 hours	**≥ 0.3** mg/dl/h	• Warning in the table

Table 8: Test criterion: rate of increase of the bilirubin value
(Legend: "<" less than; ">" greater than; "≥" greater than or equal to; "≤" less than or equal to)

7. Function test

NOTE!
Using NeoPrediX B.1 with malfunction(s)
Using NeoPrediX B.1 software that is not working properly can lead to **anomalous predictions.**
▶ Do not use the software if it is not functioning properly.
▶ Report any malfunctions to NeoPrediX AG.
▶ Use the form in the software's help function.

To check whether the NeoPrediX B.1 software is working properly, you can perform a function test.

▶ Enter the following data for a test patient:

Parameter	Value
Date of birth	e.g. 2022-10-04
Time of birth	11:30 a.m.
Gestational age	39+0
Weight at birth	3070 g
Delivery mode	Cesarean
First measurement	2022-10-05 11:30 a.m. 7 mg/dl TSB (24 hours after birth)
Second measurement	2022-10-06 11:30 a.m. 10.4 mg/dl TSB (48 hours after birth)

Table 9: Test data for function test

The diagram of the prediction of bilirubin progression should correspond to the following figure and values:

Prediction value at 108h 14.8 mg/dl to 18.5 mg/dl

If the comparison does not match:

▶ Do not continue to use the software to predict bilirubin progression.
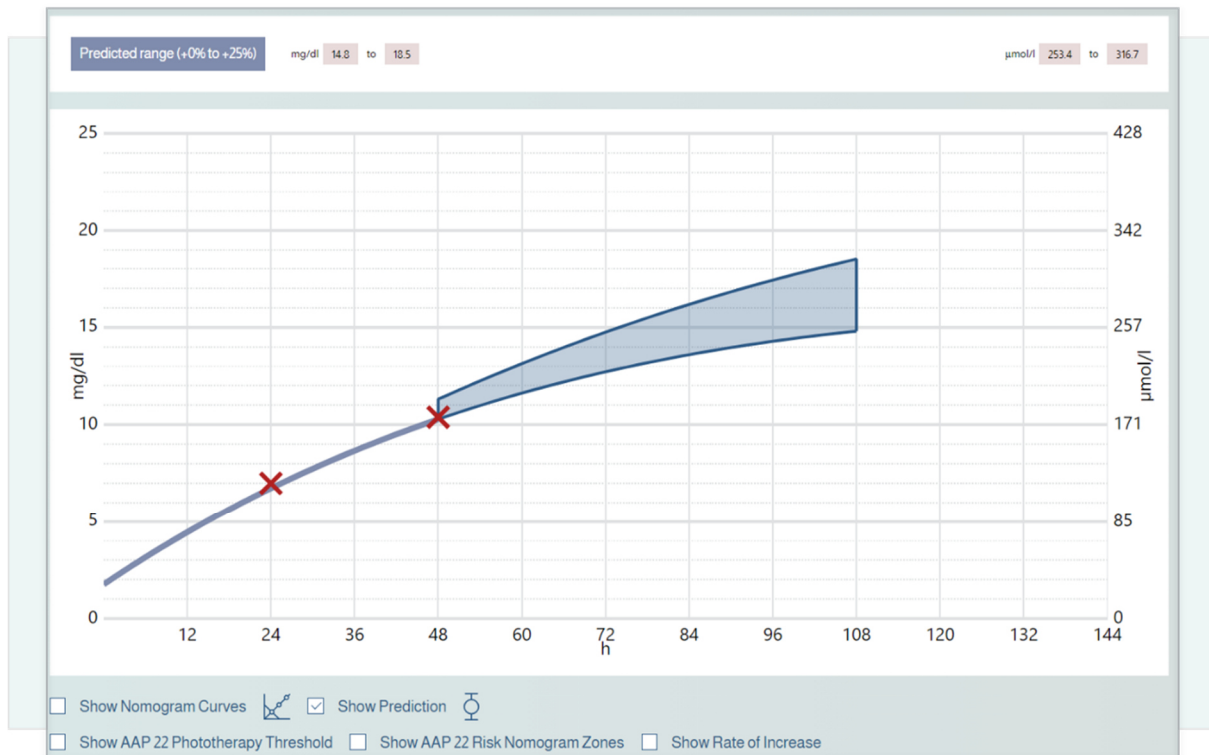
▶ Report the error to NeoPrediX AG

Figure 18: Expected result of function test

8. Cybersecurity

The operator is responsible for providing appropriate security information and a secure environment outside of the software system covered here (e.g., security of the operating system, browser, restricted physical access to certain areas of the software system's usage environment). This includes ensuring the maintenance of security during the operation and use of the software system.

> ℹ️ Special training or skills related to cybersecurity are not required for the use of the software.

Duties of the operator:

► Make sure that the necessary security levels are guaranteed for the operating environment, including the required infrastructure, such as the latest browser version, network, physical access, and up-to-date malware software (see also section 5.1).

► Use best-practice security standards.

► Make sure that the staff is properly trained and available for security issues.

► Make sure that the system is used in accordance with the manufacturer's guidelines and security requirements. Among others, these include:
  - No physical access by unauthorized users
  - Setting access rights via user roles
  - Compliance with password guidelines by users (see also section 6)
  - Disabling functions/applications that are not used and do not contribute to security (also relevant outside the software system, e.g., applications in the runtime environment)
  - Do not use mobile devices when using the software

► Make sure that health data and personal data are also protected outside of the software system (e.g., exported files or printed reports from the software).

► Make sure that the prescribed maintenance is carried out as required, including accepting the installation and provision of security updates/patches by the manufacturer.

► Inform the manufacturer and the competent authority of the Member State in which the user and/or patient is located immediately of any suspected security incident.

In the document "Technical and Organizational Measures" provided by the manufacturer, you will find further information on:

- Security-by-default principle
- Data storage
- Security checks for data protection
- Planned updates/patches
- Latest software version
- Description of the backup and update procedure by the manufacturer
- Recording of log files for security events
- Use of automatic analysis software
- Security event reports from software

9. Help

If you have any questions or problems, use the help function in the software to get assistance. You can find it in the footer of the application.

10. Contact information

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APPENDIX I

Explanations on how to determine the maximum prediction period for bilirubin progression

The number of recorded bilirubin values, the type of bilirubin values, and the timing of the measurements performed affect the maximum prediction period of bilirubin progression from the last measurement. NeoPrediX B.1 offers three different lengths (30, 48, and 60 hours) for the prediction period.

The maximum prediction period is determined based on a lead and support concept. In short, all entered bilirubin measurements are categorized as either Lead or Support. For the Lead Bilirubin measurements, the maximum prediction period is determined using three rules.

Rule 1: Prediction period with a maximum length of 30 hours

If a TSB measurement is available between 8 and 72 hours after birth, a maximum prediction of 30 hours after the last measurement is possible.

Rule 2: Prediction period with a maximum length of 48 hours

If any measurement is taken between 8 and 72 hours after birth, and another measurement is taken between 24 and 120 hours after birth, with an interval of at least 8 hours, a maximum prediction of 48 hours after the last measurement is possible. There is an exception for two TSB measurements; see the following rule 3.

Rule 3: Prediction period with a maximum length of 60 hours

If a TSB measurement is taken between 8 and 72 hours after birth, and another TSB measurement is taken between 24 and 120 hours after birth, with an interval of at least 8 hours, a maximum prediction of 60 hours after the last measurement is possible.

Additional notes for further bilirubin measurements

If further bilirubin measurements are available, they do not affect the length of the already determined maximum prediction period, but they are used to predict the bilirubin progression and thus support the prediction. These so-called support bilirubin measurements can be taken at any time between 1 and 120 hours after birth. The above stated condition regarding the minimum 8-hour interval in the rules for lead measurements does not apply to support bilirubin measurements. The distance between the lead and support for bilirubin measurement or the distance between support and additional support for bilirubin measurement is arbitrary.