User manual
for the
Beta Lactam Antibiotic Stewardship Tool (BLAST)

Version 2, November 2024, in English

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1. The Evidencio platform

The Evidencio platform facilitates the creation, use, validation and implementation of medical prediction models and clinical decision support tools. This User Manual specifically relates to the Beta Lactam Antibiotic Stewardship Tool (BLAST). The User Manual can also be referred to as the Instructions For Use (IFU).

Throughout this manual CE-marked content and the term medical device are used interchangeably.

2. Disclaimer

Evidencio provides information, models, calculators, equations, and algorithms (tools) intended for use by healthcare professionals. Some of these tools have been certified as CE-medical devices. For such CE-marked content the 'Official Legal Disclaimer for CE-marked content' applies. All other content and tools provided by Evidencio are explicitly only covered by the 'Official Legal Disclaimer for non-CE-marked content. Both are available on the Evidencio website: https://www.evidencio.com/disclaimer.

3. Warnings

3.1. Warnings for CE-marked content

Calculations alone should never dictate patient care, and are no substitute for professional judgement. This tool is only to be used by professionals, and is not suitable for use by patients on their own.

Always read the intended use before using this device.

Always make sure the patient complies with the clinical indications and clinical contra-indications as stated on the Evidencio website, and in **paragraphs 6.3.1** and **6.3.2** of this user manual respectively.

Before reading the result, double check the filled in values to prevent errors since the BLAST can retain data for the duration of the use of the BLAST. Importantly, always refresh the model after each patient to remove the data, especially when using the BLAST consecutively for multiple patients.

Results that concern risk percentages, do not guarantee certain outcomes. When there is a risk present, do not expect an event to not occur at all, even if the risk is very small. Conversely, a high risk does not guarantee that an event will occur.

This model is only intended for use in settings where the usage and result of a device are never immediately needed.

Calculations alone should never dictate patient care, and are no substitute for professional judgement. See our full disclaimer on: https://www.evidencio.com/disclaimer.

The data used to perform the calculations is stored by Evidencio to enhance model function and allow issues to be traceable for further improvements. For details, see the privacy policy on our website at: https://www.evidencio.com/privacy-policy.

4. Device Description BLAST

The BLAST is Medical Device Software (MDSW) that aims to provide information that can be used to support decisions regarding antibiotic treatment of a patient with a reported allergy for beta lactam antibiotics. The device is a dynamic decision tree that guides the user to next branch in the tree based on the patient specific data that is entered by the user. The user interface of the BLAST has been designed in such a way, that the user will be able to identify the relevant information required to complete each step of the algorithm directly on the interface. The specifics of where these details can be identified are outlined in chapter 10 of this manual.

4.1. Lifetime, residual risks and side effects

The BLAST is software, and does not expire. The lifetime is initially set at 5 years from certification, if the state of the art does not change in such a way as to negatively affect the benefit-risk of the device, the lifetime can be extended.

No steps are required to be undertaken by the user to decommission a product when it is taken off the market. If the lifetime is not extended, a notice will be placed on the model page on the platform. When a device is taken off the market, users may be informed about this (e.g. through e-mail).

Evidencio has identified a series of risks associated with the use of this model.

The BLAST is a low-risk device, there are no noticeable risks involved outside of possible mis-estimation of patient probability of a positive penicillin allergy test, and possible mis-information regarding safety of alternative antibiotics due to (possible) cross-reactivity. All residual risks are accepted.

Most risks can be defined into two main groups, depending on their outcome.

a) The risk calculation was wrong or;
b) The MDSW prediction model is inaccessible.

A wrong risk calculation can be the result of erroneous input values or an error in the mathematical calculation. Technical risks, including the erroneous calculations or the inaccessibly due to a technical error, have been mitigated when possible. These measures focussed on reducing the risks' probability and severity. Concluding that the risks could not be mitigated further, the residual risks were classified as *low-level and acceptable.* It should be noted that the use of Evidencio's Medical Device Software is itself a risk mitigation measure, as Evidencio's certified Quality Management System ensures and monitors the reliability of the calculations performed with its certified medical devices.

The BLAST does not have any direct side effects.

5. Electronic Label

The electronic label of this device contains the following information:

Name of the device	Beta-lactam Antibiotic Stewardship Tool (BLAST)
Manufacture information	Evidencio B.V., Irenesingel 19, 7481 GJ Haaksbergen, The Netherlands
LOT number	V-1.0-10628.24.11.08
UDI-PI number	08720938015274

The electronic label can be found on the Evidencio website, see also section **N** and **Figure *7***.

The electronic label on the website further contains the option to download the **User Manual** and **Declaration of conformity** (DoC).

5.1. LOT number

The LOT number indicated the model version, the model identifier, and the model publication date. Publication date is indicated as YY.MM.DD.

5.2. UDI-PI number

Stands for Unique Device Identifier Production Identifier (UDI-PI) number is an international tool that helps users identify and find information on products. Evidencio's UDI-PIs have the following format:

(01)[UDI-DI number](8012)[versionnumber](4326)[releasedate](240)[identificationnumber]

The UDI-DI (Device Identifier) number is a unique numeric code. For each medical device of Evidencio, a unique UDI-DI is ascribed. This UDI-DI is used as an "access key" for information stored in a unique device identification database (UDID). Information on Evidencio's medical devices can be found by searching for the UDI-DI number in the following data base: https://gepir.gs1.org/index.php/search-by-gtin.

6. Intended Purpose

6.1. Intended Medical Use

The BLAST is intended to be used by professional users who are capable of operating the device and interpreting its results. It can be used to support clinical decision making regarding the safe administration of beta-lactam antibiotic treatment in patients with a reported allergy for beta-lactam allergies.

The BLAST combines details regarding a previous allergic reaction (e.g. time since previous reaction, severity of the reaction, and whether a treatment was required to resolve the reaction) to provide an estimate on the probability of a positive allergy test in patients with a patient reported allergy. Of note is that the PEN-FAST and PEN-FAST+ components of the device are not intended to be used for patients under 18 years of age. For patients at higher risk of an allergy, the BLAST provides a list of safe alternative antibiotics for which no cross-reactivity with the culprit drug is evident.

The device is intended to be used for patients with a patient reported allergy. The result of the BLAST is intended to be reviewed and interpreted by qualified medical specialists only. The device is not intended for use by patients on their own.

The BLAST is not intended to replace clinical decision-making, it can only provide information to the user on the risk of a positive allergy test and on the cross-reactivity with other antibiotic treatment options. The user can use this information, in conjunction with other clinical and personal details, to support clinical decision-making regarding the treatment of the patient.

6.2. Clinical benefit

The benefits (and risks) involved with the use of the BLAST are indirect. The software is not capable of providing a direct benefit to the patient. The results of the device can be used to support decisions that will benefit the patient. Correct functioning of the BLAST can eventually result in these clinical benefits:

- The BLAST can assist in risk stratification for patients
- Risk stratification can reduce the burden of (invasive and intensive) medical procedures such as tests on patients with low risks, reducing, shortening or avoiding stays in hospitals or other care facilities.
- Risk stratification can reduce the unnecessary consumption of (scarce) medical resources, decreasing costs and increasing their availability for high risk patients.
- Digital implementation of the algorithm underlying the BLAST as a medical device can improve the speed and reliability of calculation. For the beta-lactam selector component, this can result in an improved speed and reliability of determining possible cross-reactivity with other antibiotic treatment options. This would further increase the accuracy of the prognosis and by extension increase the chance for the above-mentioned benefits.

6.3. Indented target population and exclusion

The BLAST is intended to be used only for a specific group of patients, corresponding to the indications and contra-indications shown below.

6.3.1. Clinical indications

The BLAST should be used for patients who meet the following inclusion criteria:

- Suspected or confirmed beta-lactam antibiotic allergy**.**

6.3.2. Clinical contra-indications

The PEN-FAST and PEN-FAST+ are not validated in children and are not intended for use in patients under 18 years old.

6.4. User profile

The BLAST is intended to be used by Healthcare Professionals. Results shall always be reviewed and interpreted by qualified professionals who are able to prescribe or administer antibiotics, in the context of the patient's clinical history and other diagnostic test results. Healthcare professionals do not require additional training prior to the use of the medical device. The device is not intended for use by lay persons on their own.

6.5. Intended use environment

The MDSW can be used as made available on the Evidencio platform in any actively supported web-browser on personal computers, mobile devices, or tablet PCs, and on the mobile app provided by Evidencio. The MDSW can also be used through Evidencio's iFrame representation as an embedded view, provided that the specific Evidencio guidelines for iFrame implementations of this MDSW are adhered to. The device is only intended for use in healthcare settings where the immediate application and outcomes of the device are not required.

6.6. Physical interaction

The MDSW is stand-alone software and does not come into contact with any bodily or other material of the patient, user or otherwise.

6.7. Versions of the MDSW

The version of the BLAST concerns the initial version of MDSW of which Evidencio is the manufacturer.

6.8. Functioning, physical principle

The MDSW's underlying mathematical formula is a custom sequential model. The acquisition and processing of the data, the analyses to assemble the relevant criteria for the MDSW as well as the setup and refinement of the BLAST are provided in the instructions for use. Entering the details for an individual in the MDSW initiates the estimation of the risk for a positive allergy test, which is provided to the user together with accurate information of cross reactivity with other antibiotic treatment options when a patient is allergic.

7. Result interpretation

The outcome of the BLAST will vary depending on the input. Users will be presented with one or more of the following outcomes:

1. For the PEN-FAST, the number of points, risk stratification and risk percentage of true penicillin allergy is given for very low risk (<1%), low risk (5%), moderate risk (20%) or high risk (50%), in some cases accompanied by extra instructions or background information.
2. For the PEN-FAST+, the number of points, risk stratification and risk percentage of true penicillin allergy is given for very low risk (<2%), low risk (±6%), moderate risk (±28%) or high risk (±80%), in some cases accompanied by extra instructions or background information.
3. Feedback about the input provided to calculate the PEN-FAST or PEN-FAST+.
4. Guidance for clinical decision-making, e.g. to perform a direct oral penicillin challenge, a drug provocation test, (de)labelling, referral to an allergy specialist, relative contra-indications, intended use of the BLAST, risk assessment of the BLAST, classification of the adverse reaction, remarks about scientific literature and suggestion to use the PEN-FAST or PEN-FAST+.
5. For the Beta-lactam selector, a list of alternative antibiotics that are either safe or unsafe for the patient due to possibilities of cross-reactivity, based on cross-reactivity literature. If the variable "Familiarity beta-lactam allergy" is answered with "much experience", the user can choose to show discrepancies, i.e. alternative antibiotics for which discrepancies exist in the cross-reactivity literature used to create the Beta-lactam selector. Unless "yes" is answered for "Display discrepancy details", alternative antibiotics for which discrepancies exist will be shown under "Potential cross-reactivity".
6. A schematic from an EAACI position paper depicting a flow-chart algorithm for management of antibiotic allergies from Barbaud *et al*. (2024).
7. References of scientific literature and guidelines that contributed to the BLAST and/or describes recommendations towards the management of antibiotic allergies.

Conditional information

Calculations alone should never dictate patient care, and are no substitute for professional judgement. See the Evidencio website for the full disclaimer; https://www.evidencio.com/disclaimer.

8. Additional information

8.1. Details

Model author:	Dr. R.G. Pleijhuis
Root model ID	10628
Version	1.0
Revision date	11-NOV-2024
Speciality	Emergency medicine, General practice, Infectious disease, Intensive care, Internal medicine, Microbiology, Surgery
Model type	Sequential model
MeSH terms	• Antibiotic Stewardship • Anaphylaxis • Skin Rash • Skin Tests • Drug Allergy • Beta-Lactams

8.2. Input variables

The calculator combines patient data with clinical data and lab results to calculate the probabilities. Input variables are required to determine the results of the model. The outcomes of the BLAST are calculated using a sequential model based on six others. To perform the calculations successfully, the BLAST requires the input variables as listed in **Tables 1** to **6.**

Table 1. Variables used as input for the PEN-FAST decision rule.

Name	Description	Type	Options
Reaction occurred ≤5 years ago	Describes the time that has passed since previous reaction	Categorical	No/Yes
Anaphylaxis	Describes whether there is anaphylaxis	Categorical	No/Yes
Angioedema	Describes whether there is angioedema (Only becomes visible when the variable “Anaphylaxis” is set to “no”.)	Categorical	No/Yes
Severe cutaneous adverse reaction (SCAR)	Describes whether there is a severe cutaneous adverse reaction (SCAR)	Categorical	No/Yes
Treatment required for reaction	Describes whether a treatment was required to resolve the reaction	Categorical	No/Yes/Unknown

Table 2. Variables used as input for the Adapted PEN-FAST+ (‘Plus’) Prediction algorithm.

Name	Description	Type	Options
Reaction occurred ≤5 years ago	Describes the time that has passed since previous reaction	Categorical	No/Yes
Anaphylaxis	Describes whether there is anaphylaxis	Categorical	No/Yes
Angioedema	Describes whether there is angioedema (Only becomes visible when the variable “Anaphylaxis” is set to “no”.)	Categorical	No/Yes
Severe cutaneous adverse reaction (SCAR)	Describes whether there is a severe cutaneous adverse reaction (SCAR)	Categorical	No/Yes

Skin rash lasting >7 days	Describes whether there was a skin rash that lasted for more than 7 days.	Categorical	No/Yes
Immediate reaction within 1 hour	Describes whether there was an immediate type reaction (e.g. urticaria) occuring in <1 hour?	Categorical	No/Yes

Table 3. Variables used as input for the PEN-FAST decision rule (no SCAR).

Name	Description	Type	Options
Reaction occurred ≤5 years ago	Describes the time that has passed since previous reaction	Categorical	No/Yes
Anaphylaxis	Describes whether there is anaphylaxis	Categorical	No/Yes
Angioedema	Describes whether there is angioedema (Only becomes visible when the variable "Anaphylaxis" is set to "no".)	Categorical	No/Yes
Treatment required for reaction	Describes whether a treatment was required to resolve the reaction	Categorical	No/Yes

Table 4. Variables used as input for the Adapted PEN-FAST+ ('Plus') Prediction algorithm (immediate reaction).

Name	Description	Type	Options
Anaphylaxis	Describes whether there is anaphylaxis	Categorical	No/Yes
Angioedema	Describes whether there is angioedema (Only becomes visible when the variable "Anaphylaxis" is set to "no".)	Categorical	No/Yes
Reaction occurred ≤5 years ago	Describes the time that has passed since previous reaction	Categorical	No/Yes

Table 5. Variables used as input for the PEN-FAST+ ('Plus') Prediction algorithm (delayed reaction).

Name	Description	Type	Options
Anaphylaxis	Describes whether there is anaphylaxis	Categorical	No/Yes
Reaction occurred ≤5 years ago	Describes the time that has passed since previous reaction	Categorical	No/Yes

Table 6. Variables used as input for the Alternative beta-lactam selector tool based on chemical composition.

Name	Description	Type	Options	
When 'Familiarity beta-lactam allergy' is set to 'limited experience'/'some experience' and 'Urgent need for an antibiotic' is set to 'yes' OR 'much experience' and 'Select safest alternative beta-lactams based on chemical composition' are selected				
Select from quicklist	Describes which antibiotics are a suspected culprit from a short list	Categorical	Amoxicillin [Amoxil] (J01CA04) Amoxicillin/clavulanic acid [combination] (J01CR02) Cefazolin [Ancef, Kefzol] (J01DB04) Ceftazidime [Fortaz, Tazicef] (J01DD02) Ceftriaxone [Rocephin] (J01DD04) Cefuroxime [Ceftin, Zinacef] (J01DC02) Flucloxacillin (J01CF05)	Penicillin V [phenoxymethylpenicillin] (J01CE02) Penicillin [not otherwise specified] (J01C) - Piperacillin/tazobactam [combination] (J01CR05) All options can be selected independently by checking boxes.

			Penicillin G [Benzylpenicillin] (J01CE01)	The number of selected options is summed.
Other beta-lactams (optional)	Describes other beta-lactams which can be selected as a suspected culprit from a list	Categorical	Ampicillin (J01CA01) Aztreonam (J01DF01) Cefaclor (J01DC04) Cefadroxil (J01DB05) Cefamandole (J01DC03) Cefetamet [J01DD10] Cefatrizine (J01DB07) Cefdinir (J01DD15) Cefditoren (J01DD16) Cefepime (J01DE01) Cefiderocol (J01DI04) Cefixime (J01DD08) Cefodizime (J01DD09) Cefonicid (J01DC06) Cefoperazone (J01DD12) Ceforanide (J01DC11) Cefotaxime (J01DD01) Cefotetan (J01DC05) Cefotiam (J01DC07) Cefoxitin (J01DC01) Cefpodoxime (J01DD13) Cefpirome (J01DE02) Cefprozil (J01DC10)	Ceftaroline (J01DI02) Ceftezole (J01DB12) Ceftizoxime (J01DD07) Ceftobiprole (J01DI01) Ceftolozane (J01DI54) Cefradine (J01DB09) Ceftibuten (J01DD14) Cefalexin (J01DB01) Cefalotin (J01DB03) Cefapirin (J01DB08) Dicloxacillin (J01CF01) Ertapenem (J01DH03) Imipenem (J01DH51) Loracarbef (J01DC08) Meropenem (J01DH02) Nafcillin (J01CF06) Oxacillin (J01CF04) Pivmecillinam (J01CA08) Pheneticillin (J01CE05) Piperacillin (J01CA12)
Show overview of safe(st) beta-lactam alternatives	Describes whether alternatives should be displayed	Categorical	No / Yes	
Display discrepancy details	Describes whether discrepancy details should be displayed (only available when 'much experience' was selected)	Categorical	No / Yes	
When 'Familiarity beta-lactam allergy' is set to 'limited experience'/'some experience' and 'Urgent need for an antibiotic' is set to 'no' OR 'much experience' and 'Stratify risk of (suspected) penicillin allergy in patients ≥18 years old' are selected				
Penicillin selection list (Select to which penicillin antibiotic the patient reacted (suspected culprit))	Describes which penicillin antibiotics are a suspected culprit	Categorical	Amoxicillin (J01CA04) Amoxicillin/clavulanic acid [combination] (J01CR02) Ampicillin (J01CA01) Dicloxacillin (J01CF01) Pheneticillin (J01CE05) Flucloxacillin (J01CF05) Nafcillin (J01CF06) Oxacillin (J01CF04) Penicillin G [benzylpenicillin] (J01CE01) Penicillin V [phenoxymethylpenicillin] (J01CE02)	Penicillin [not otherwise specified] (J01C) Piperacillin (J01CA12) Piperacillin/tazobactam [combination] (J01CR05) Pivmecillinam (J01CA08) All options can be selected independently by checking boxes. The number of selected options is summed.

Add non-penicillin beta-lactam(s) (Add additional (suspected) non-penicillin culprit(s) (if available))	Describes which non-penicillin beta-lactam(s) are a suspected non-penicillin culprit	Categorical	Aztreonam (J01DF01) Cefaclor (J01DC04) Cefadroxil (J01DB05) Cefamandole (J01DC03) Cefetamet [J01DD10] Cefatrizine (J01DB07) Cefazolin (J01DB04) Cefdinir (J01DD15) Cefditoren (J01DD16) Cefepime (J01DE01) Cefiderocol (J01DI04) Cefixime (J01DD08) Cefodizime (J01DD09) Cefonicid (J01DC06) Cefoperazone (J01DD12) Ceforanide (J01DC11) Cefotaxime (J01DD01) Cefotetan (J01DC05) Cefotiam (J01DC07) Cefoxitin (J01DC01) Cefpodoxime (J01DD13) Cefpirome (J01DE02) Cefprozil (J01DC10) Ceftaroline (J01DI02) Ceftazidime (J01DD02)	Ceftezole (J01DB12) Ceftizoxime (J01DD07) Ceftobiprole (J01DI01) Ceftolozane (J01DI54) Cefradine (J01DB09) Ceftriaxone (J01DD04) Ceftibuten (J01DD14) Cefuroxime (J01DC02) Cefalexin (J01DB01) Cefalotin (J01DB03) Cefapirin (J01DB08) Ertapenem (J01DH03) Imipenem (J01DH51) Loracarbef (J01DC08) Meropenem (J01DH02) All options can be selected independently by checking boxes. The number of selected options is summed.
Show overview of safe(st) beta-lactam alternatives	Describes whether alternatives should be displayed	Categorical	No / Yes	
Display discrepancy details	Describes whether discrepancy details should be displayed (only available when 'much experience' was selected)	Categorical	No / Yes	

Formula

The following formulas are used for the different components of the BLAST:

- **PEN-FAST decision rule:**

PEN-FAST Score = Reaction occurred ≤5 years ago + Anaphylaxis + Angioedema + Severe cutaneous adverse reaction (SCAR) + Treatment required for reaction

- **Adapted PEN-FAST+ ('Plus') prediction algorithm:**

  PEN-FAST+ Score = Reaction occurred ≤5 years ago + Anaphylaxis + Angioedema + SCAR + Skin rash lasting >7 days + Immediate reaction within 1 hour

- **PEN-FAST decision rule (no SCAR):**

PEN-FAST (no SCAR) Score = Reaction occurred ≤5 years ago + Anaphylaxis + Angioedema + Treatment required for reaction

- **Adapted PEN-FAST+ ('plus') prediction algorithm (immediate reaction):**

PEN-FAST+ (immediate reaction) Score = Reaction occurred ≤5 years ago + Angioedema + 2 Importantly, 'Angioedema' is available only if 'Anaphylaxis' is 'no'.

- **PEN-FAST+ ('plus') prediction algorithm (delayed reaction):**

PEN-FAST+ (delayed reaction) Score = Reaction occurred ≤5 years ago + Angioedema + 2

- **Alternative beta-lactam selector tool based on chemical composition:**

The Beta-lactam selector model does not contain a formula and relies on a R-script.

8.3. Study characteristics

The PEN-FAST decision rule was developed with a cohort that consisted of 622 patients in a multicenter prospective antibiotic allergy–tested cohort from 2 tertiary care sites in Melbourne, Australia (Austin Health and Peter MacCallum Cancer Centre) and validated in three cohorts from Sydney and Perth, Australia, and Nashville, Tennessee, that combined consisted of 945 patients by Trubiano et al. Further external validation was performed, among others, in a single-centre, retrospective cohort analysis of 142 patients by Piotin et al. and a prospective cohort of 252 patients by Castagna et al. that was also used for the development and validation of the PEN-FAST+.

In the tables **Table 7**/**Table 8** information on the characteristics of the patient data used to derive the PEN-FAST model is provided, in the tables **Table 9**/**Table 10** information on the characteristics of the patient data used to validate the PEN-FAST model is provided.

Table 7. This table contains information on the patient group data used to derive the PEN-FAST decision rule.

Name	Median	IQR	Unit
Age	60	48-71	Years
No. of allergy labels	1	1-2	-

Table 8. This table contains categorical characteristics on the patient group data used to derive the PEN-FAST decision rule.

Name	Number of patients
Female	367 (59.0%)
Penicillin allergy labels	
Penicillin VK, G or unspecified	443 (71.2%)
Amoxicillin or ampicillin	117 (18.8%)
Flucloxacillin or dicloxacillin	29 (4.7%)
Combined amoxicillin and clavulanate potassium	33 (5.3%)
Allergy phenotypes	
Non-immune mediated (type A)	15 (2.4%)
Immediate immune-mediated (type B1)	268 (43.1%)
Delayed immune-mediated (type B4)	206 (33.1%)
SCAR	5 (0.8%)
Rash unspecified	46 (7.4%)
Concurrent Cephalosporin allergy label	116 (18.6%)
Immunocompromised	347 (55.8%)
History of mental illness	88 (14.1%)
Intradermal test performed	468 (75.2%)
Skin prick test performed	498 (80.1%)
Patch test performed	8 (1.3%)
Oral challenge	
Overall oral challenge performed after skin testing	459 (73.8%)

Oral challenge performed after skin testing in the outpatient setting (% of overall)	456 (99.3%)
Overall direct oral challenge (no skin testing performed)	167 (26.8%)
Direct oral challenge performed in the outpatient setting (% of overall)	26 (15.6%)
Any positive allergy test finding	60 (9.6%)
Positive penicillin allergy test finding	58 (9.3%)

Table 9. This table contains information on the patient group data used to validate the PEN-FAST decision rule.

Name	Median	IQR	Unit
Age	55	39-67	Years

Table 10. This table contains categorical characteristics on the patient group data used to validate the PEN-FAST decision rule.

Name	Subtypes/answer options	Number of patients
Sex	**Female**	302 (68.2%)
Allergy phenotypes		
Immune mediated		
	SCAR	4 (0.5%)
	Angioedema/Anaphylaxis	110 (27.1%)
	Other	299 (63.8%)
Non-immune mediated		4 (4.9%)
Unknown		5 (3.6%)
Treatment for allergy	Yes	93 (20.9%)
	No	127 (31.7%)
	Unknown	203 (47.3%)
Time from reaction <5 years		188 (34.6%)
Skin prick and intradermal testing		422 (99%)
Oral challenge		405 (89.3%)
Any penicillin allergy test positive		30 (17.1%)
IDT		25 (12.4%)
Oral challenge		5 (6.2%)

In the tables **Table 11**/**Table 12** information on the characteristics of the patient data used to derive and validate the PEN-FAST+ model is provided.

Table 11. This table contains information on the patient group data used to derive the PEN-FAST+ decision rule.

Name	Median	IQR	Unit
Age	51	-	Years
No. of allergy labels	1	1-2	-

Table 12. This table contains categorical characteristics on the patient group data used to derive the PEN-FAST+ decision rule.

Name	Number of patients
Female	182 (72.2%)
Immediate hypersensitivity	60 (23.7%)
Delayed hypersensitivity	95 (37.8%)
Unclassifiable hypersensitivity	97 (38.5%)

8.4. Supporting publication & Related files

Several relevant studies, such as the original derivation study by Trubiano et al. (2020) are contained in **Table 13**. These publications have tags to identify their link with the model. Examples of relevant tags are; "Peer review", "Internal validation", "External validation", and "TRIPOD". Publications that have the tags: "Internal validation" or "External validation", contain data on the performance characteristics of the device.

Table 13. Overview of selection of supporting publications & Related files.

Derivation and validation study PEN-FAST decision rule	**Development and validation of a penicillin allergy clinical decision rule** *Trubiano, Vogrin, Chua, Bourke, Yun, Douglas, Stone, Yu, Groenendijk, Holmes and Phillips* DOI: 10.1001/jamainternmed.2020.0403
Validation study PEN-FAST decision rule	**Predictive factors of amoxicillin immediate hypersensitivity and validation of PEN-FAST clinical decision rule** *Piotin, Godet, Trubiano, Grandbastien, Guénard-Bilbault, de Blay and Metz-Favre* DOI: 10.1016/j.anai.2021.07.005
Derivation and validation study PEN-FAST+	**Assessing delayed penicillin hypersensitivity using the PEN-FAST+ score** *Castagna, Chasset, Autegarden, Le Thai, Amsler, Barbaud and Soria* DOI: 10.3389/falgy.2023.1302567

8.5. Release notes

The release notes for each publicly available version of the device can be found on the Evidencio website page for the BLAST: https://www.evidencio.com/models/show/10628, selecting the correct device, and clicking on Release Notes. It is recommended to read these notes after a version update to see if these changes are relevant to you. Please make sure the correct model version is selected.

9. Using the model on the Evidencio website

Using the tool on the Evidencio website requires a stable internet connection. The tool was developed to work on the lastest versions, as of the making of this manual, of the four most commonly used internet browsers; Google Chrome, Mozilla Firefox, Microsoft Edge, and Apple Safari.

The tool can also be accessed on mobile devices running the most recent versions of the Android iOS operating systems.

Correct functioning of the tool with earlier versions of these browsers cannot be guaranteed.

The medical device cannot be used in combination with Internet Explorer. The personal computers, laptops, tablets or smartphones used should at least be able to have an internet connection and use the browsers mentioned above. The minimal screen resolution should be 800x600.

Furthermore, the model may be used through the Evidencio iFrame representation of the calculator, as an embedded view, provided that the specific Evidencio guidelines for iFrame implementations of that model are adhered to.

The Evidencio MDSW models can be used with any browser settings that don't distort the regular display of websites, with a 50% to 500% zoom rate, and at a display resolution starting from 800x600. However, factory recommended browser settings, 100% zoom rate and regular display resolution are recommended.

The MDSW is intended for authorised users only, and should not be used by unauthorised personnel.

This model is only intended for use in settings where the usage and result of a model are never immediately needed.

9.1. Landing page

The medical device model on the Evidencio platform is shown in **Figure 1**. The landing page contains the following sections, that are indicated in **Figure 1**.

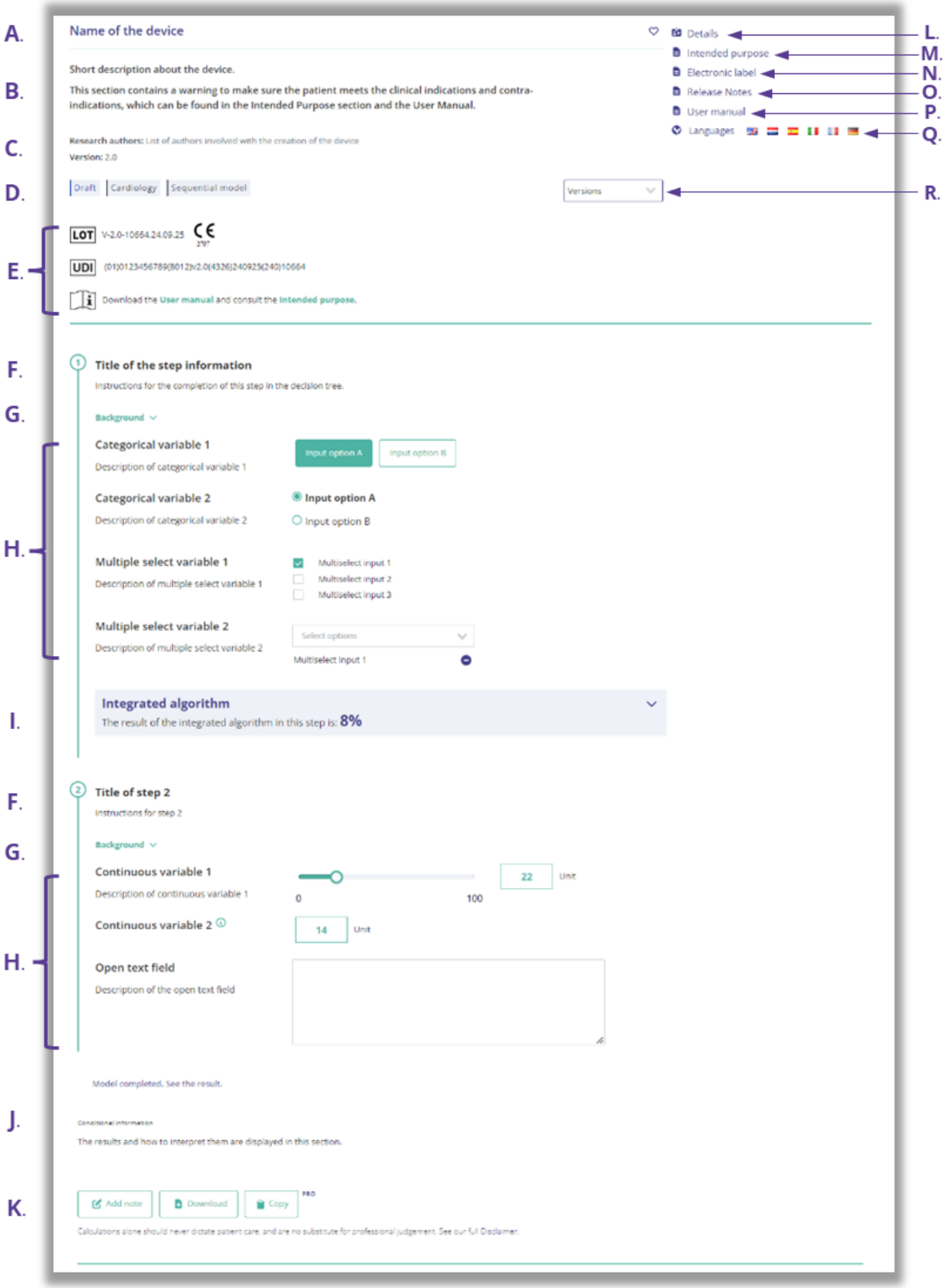

Figure 1: Screenshot of a typical landing page for Evidencio's "sequential" devices.

A. Device title

This is the title and name of the device

B. Device description

This is a short description of the device.

C. Research Authors

This is a reference to the researchers who were involved in the creation and/or validation of the device or were involved as (co-)authors of the scientific publications that were used as evidence for the development of the device.

D. Model tags

These are the tags that are assigned to the model. Evidencio has the following status tags: “Draft”, “Public”, “Private”, “Under review”. Evidencio has the following model type tags: “Composite model”, “Sequential model”, “API model”. Evidencio has the following calculation method tags: “Linear model”, “Logistic regression”, “Cox regression”, “RScript” and “Custom model”. Next to this, there are tags that indicate the specialty e.g. “Cardiology”.

E. Labels

LOT number

The LOT number indicated the model version, the model identifier, and the model publication date. Publication date is indicated as YY.MM.DD.

Additionally, the CE mark is displayed next to the LOT number. This way, medical devices can be easily recognized.

UDI-PI Number

For information on the UDI-PI Number see **Section 5.2** on **page 4** of this user manual.

Reference to the instructions for use

This sentence contains a reference to the user manual and to the intended purpose description of the device.

F. Step details

The device is set-up like a decision tree. The first step will always be the same, but the subsequent steps are defined based on the provided input. At the beginning of each step, the title of that step is displayed in bold text, and a brief description of the context of the step is provided directly below this title.

G. Background

Additional background information is provided in this step. The information is by default hidden and can become visible by clicking on: **Background** v.

H. Input parameters

Evidencio allows multiple types of input variables with different user interfaces per type of variable.

Categorical variables

In the example shown in shown in **Figure 2** and **Figure 3**, the example **Categorical Variable 1** concerns a categorical variable. The input that is wished to be used can be entered by clicking on either button. The selected button changes to green, as seen in **Figure 3**.

Figure 2. Example of categorical variables, no button has been clicked and thus no input has been provided by the user.

Figure 3. Example of categorical variables, where the "Yes" and the "Input option A" buttons have been selected.

Continuous variables

In the example shown in **Figure 4**, the **Continuous Variable 3**, exemplifies a continuous variable. The plausible ranges for which the model is tested and deemed valid are used.

The details for a patient can be entered by sliding the button to the correct value, or by entering the correct value in the box on the right-hand side (i.e., where the 10.2 mg/dL is entered for the **Continuous Variable 3**). Note that the slider is optional and therefore not available for all continuous variables.

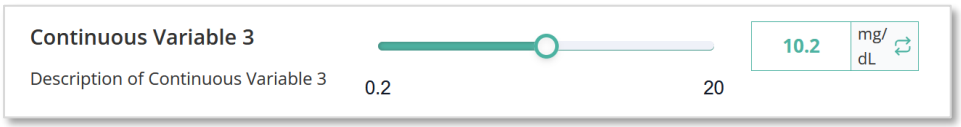

Figure 4. Example of a continuous variable, where "10.2 mg/dL" has been entered.

Unit conversion

Sometimes it is possible to use a unit conversion, by clicking on the unit when the green arrows are present. See **Figure 5** below where the unit has been clicked and switched.

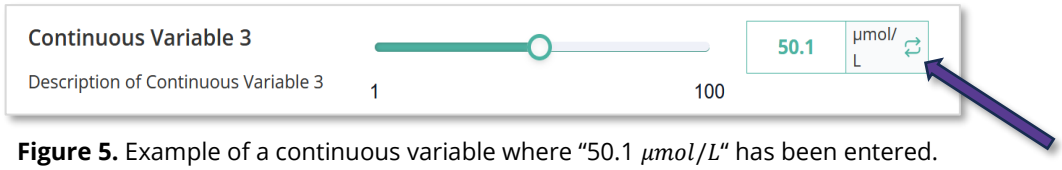

Figure 5. Example of a continuous variable where "50.1 $\mu mol/L$" has been entered.

Open text field

Text variables allow users to enter any text as input. **Figure 6** displays an open text field variable.

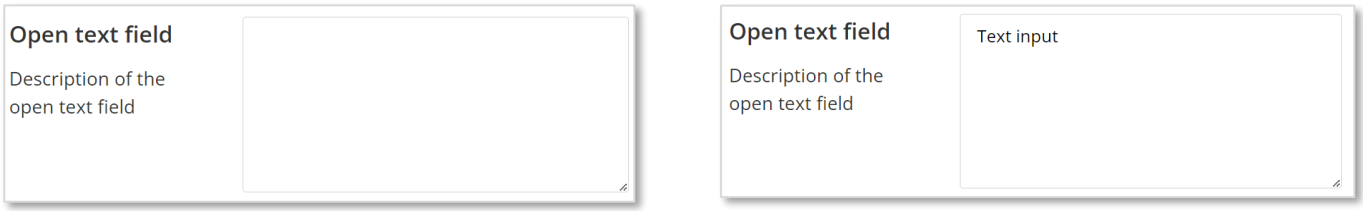

Figure 6. Example of an open text field variable where no input has been provided (left), and where "Text input" was entered (right).

Variable descriptions.

Directly underneath the name for each variable, additional details can be provided on the methods required to enter the correct value for each variable. Details may include but are not limited to; more detailed explanation of the variable, the ranges of the variables (for healthy individuals), or a description when a continuous variable should be true or false. Details may be truncated or completely hidden behind this icon: ⓘ Hover over this icon to see the full details.

I. Integrated algorithm results

At the end of a step, the results of an underlying integrated algorithm may be displayed. Such results are not available within each step, and multiple algorithms can be integrated in a step. Specific details related to the results of the algorithm can be identified by clicking on the **v** at right hand side of the box in which the results are displayed.

J. Result interpretation

At the bottom of the page, the results of the model are shown.

Calculations alone should never dictate patient care, and are no substitute for professional judgement. See our full disclaimer on: https://www.evidencio.com/disclaimer.

Result calculation

When all variables are filled in, a result will be calculated. No result is displayed until all variables are filled in and the result section will indicate; *"Set all parameters to calculate prediction."*

Result interpretation

In the result interpretation, a stratification may be provided based on the calculated results. Additional information about this stratification and the classification as found in the derivation and important validation cohorts may also be provided. An example of the information is shown in **Figure 6**.

K. Saving the results & the disclaimer

Add Notes

Click on this button to add a note that is specific to the input provided. The note will be included when the results will be downloaded or copied.

Download results as PDF

Click on this button to download the results as a .pdf.

Copy the results

Click on this button to copy all the results to your clipboard. The results can then be pasted in e.g. a Word file, or directly in a patient health record.

Disclaimer

At the bottom of each Medical Device page hosted by Evidencio, the following Disclaimer is provided: "*Calculations alone should never dictate patient care, and are no substitute for professional judgement.*" The full disclaimer is available at https://www.evidencio.com/disclaimer.

L. Details button

On the top right of the device page, several clickable buttons are. The first button opens a pop-up concerning additional information about the implementation of the device on the Evidencio platform. These details include information such as the author of the device on Evidencio, the version specific ID, the revision date, the specialties, model type, attached MeSH terms, supporting publications, other related files, and the decision tree structure of the device.

M. Intended purpose

Under this tab, the intended purpose can be found, containing information regarding the intended use, user, use environment, target population, and medical claims. This information is also provided in this manual and can be found in **Chapter 6**.

N. Electronic label

The electronic label button opens a pop-up with the location and address of Evidencio, the LOT number, the UDI number, the CE-mark, the medical device logo and a download link for the declaration of conformity of the medical device. An example of the electronic label is shown in **Figure 7**.

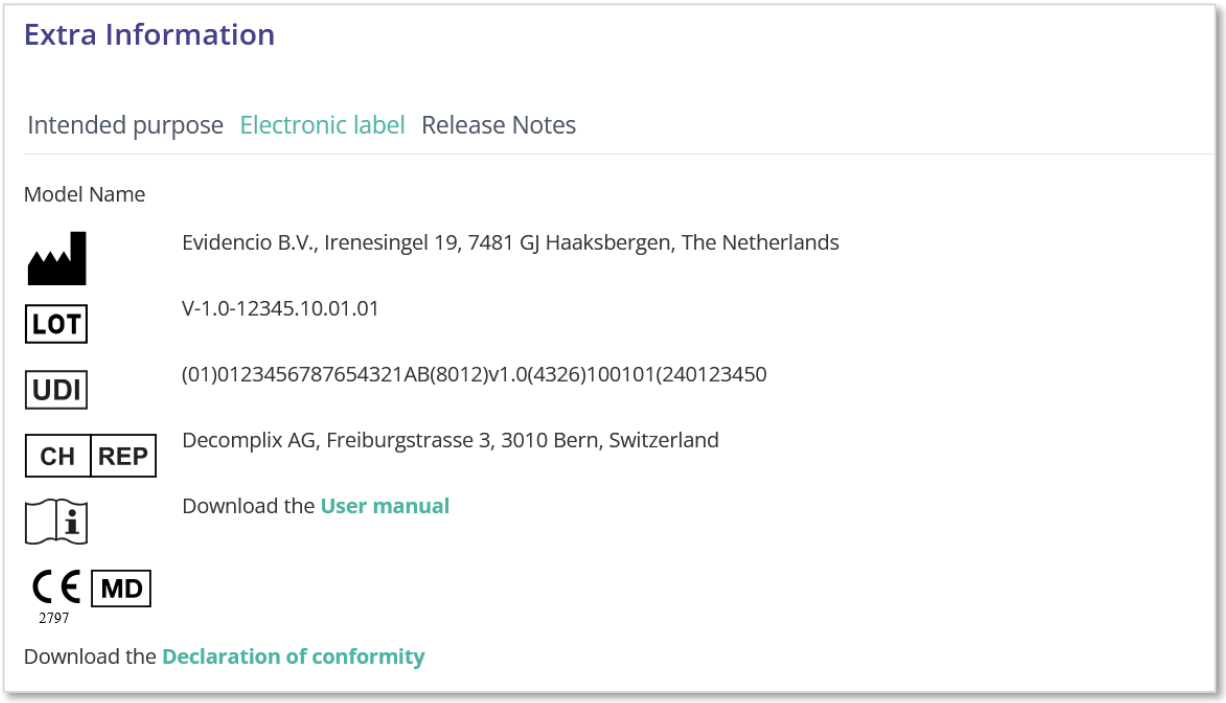

Figure 7. Example of an electronic label under the Electronic Label tab.

O. Release notes

The 'Release Notes' button opens a pop-up with the latest release notes of the model. Here you can find a list of the most significant changes over the different versions of the model. Additionally, if there are any known residual anomalies the user should be aware of, they are listed here. It is recommended to read these notes after a version update to see if these changes are relevant.

P. User manual

This user manual can be found in three places: 1) under the short description of the model on the Evidencio model page, 2) on the right of the model page, and 3) as a tab in the electronic label screen. Additionally, all versions of the user manual can be found in the general page for all user manuals for medical devices. The page can be found under the 'About' drop-down menu button as shown in **Figure 8**. The user manual page is shown in **Figure 9**. This version of the manual can be

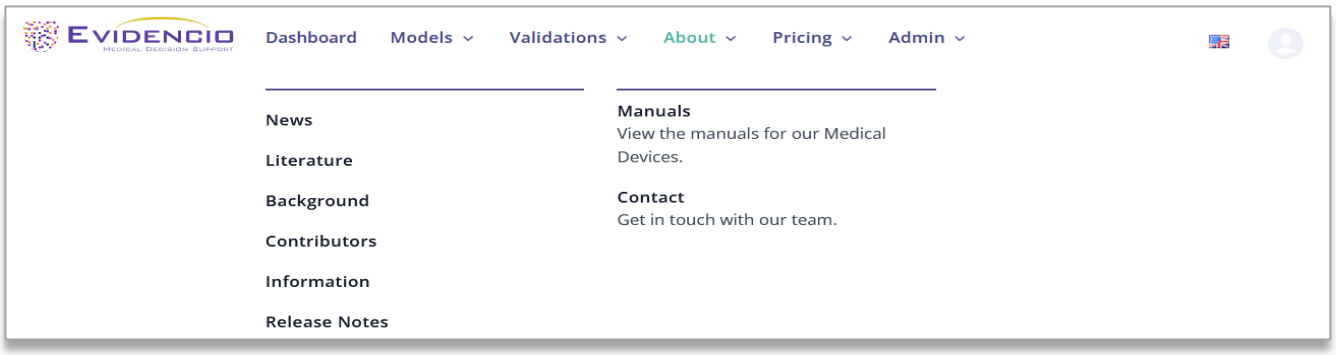

Figure 8. The drop-down menu where the user manual page can be found.

printed if required. If necessary, a paper version of the manual can be requested to be sent to you by mail. Evidencio's contact details are listed in **Chapter 10** of this user manual.

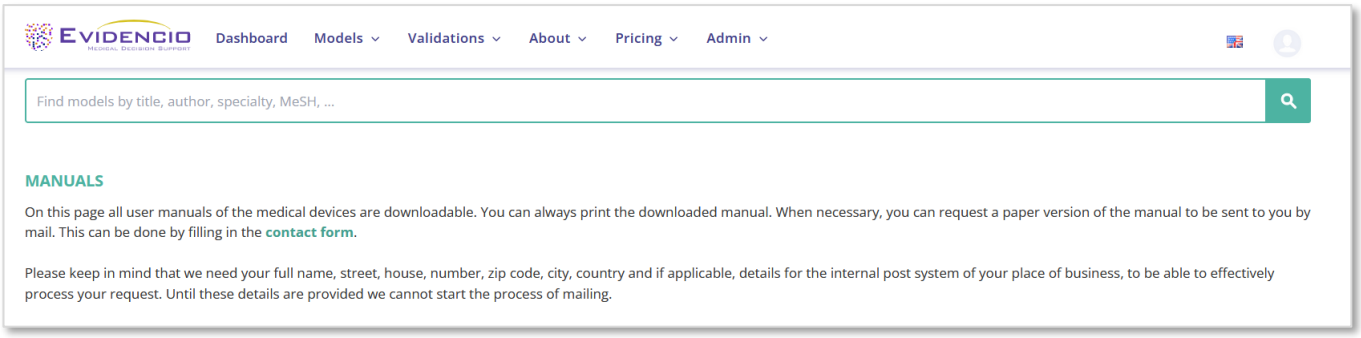

Figure 9. The user manual page for all user manuals.

Q. Languages

Here an overview of languages in which the BLAST is available is provided, any of which can be selected by clicking on the corresponding flag icon. The standard language on the Evidencio website is English. When other languages are available, these can be selected here.

Please note that, if a language is selected, only the user interface of the specific model will be translated, other general features and information on the site might still be set to one of our primary languages English, German, and Dutch.

When you find mistranslations, irregularities, confusing or ambiguous use of language in English or any other language on the Evidencio website or in one of our manuals, please do not hesitate to contact us using the contact information provided at the end of this manual.

R. Version selection

If available, clicking on the Version tab allows the user to select a different version of the BLAST for a list as displayed in **Figure 10**. Please note that the device currently selected is not presented in the dropdown menu.

Figure 10. Example of version selection tab.

10. Manufacturer details

Any serious incident that has occurred in relation to the device should be reported to the manufacturer and the competent authority of the country in which you, the reader, are established. A competent authority is the institute that governs all issues related to medical devices in a country.

Please contact Evidencio when you suspect any malfunction or changes in the performance of a medical device. Do not use the device, until Evidencio replies to your message that it is safe to start using it again.

Contact details of Evidencio:

Evidencio B.V., Irenesingel 19, 7481 GJ Haaksbergen, The Netherlands
www.evidencio.com
tel: +31 53 85195 08
e-mail: info@evidencio.com