Issued by (Name/Signature)
Erik Rehn

Date
2025-09-30

Approved by (Name/Signature)

Date

RECORD HISTORY			
VER	**CHANGE**	**ISSUED BY**	**DATE**
1A	First daft issue. Rework of the IFU for the US market based on requirements by the FDA.	Erik Rehn	2024-04-20
1B	Second draft version.	Erik Rehn	2025-09-30

START OF THE CORE TEXT

USER MANUAL

Model: FL-100

Page: 03 English

Get started by downloading the app “Flow - Depression treatment”.

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Table of Contents

Instruction for Use

- Instructions on how to use the Flow FL-100 headset and the accompanying smartphone app.
- IFU Version and Issuing date: Ver 01 - yyyy-mm-dd - DRAFT
- Product model: FL-100.
- The latest version of this manual is also available to download from flowneuroscience.com.

1. Manufacturer

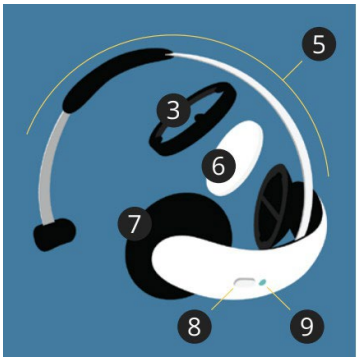
Flow Neuroscience AB
Södra Tullgatan 3
211 40 Malmö, Sweden

2. Intended use

- FL-100 is intended for the treatment of moderate to severe major depressive disorder in the current episode either as monotherapy or as an adjunctive treatment, in adult patients (18 and older) who are not considered treatment refractory to medication.
- For prescription use only (Rx only).

3. Box contents & the Headset (see Figures below)

1. Instructions for Use
2. Charger & cord
3. Two Pad Holder Rings
4. Headset
5. Metal arch
6. Pads
7. Electrodes
8. Button
9. LED indicator
10. Charger port cover
11. Back piece



After each use, put the headset and other parts back into the box.

4. Accessories

ACCESSORIES	
ITEMS	**DEFINITION**
HEADSET PADS	A BOX OF HEADSET PADS CONTAINING 20 POUCHES (SINGLE USE)
USB CHARGER	A CHARGER AND CORD

More Pads can be ordered online at flowneuroscience.com.

Reuse of pads may cause skin damage. Always start a stimulation session with a new pair of Headset pads.

5. Contraindications

Do NOT use the device in case you have:

- Open wounds, broken skin, or damaged skin at the electrode site.
- Metallic skull reconstruction at the electrode site.

6. Precautions

The device should only be used by people at least 18 years old who are diagnosed with depression (Major Depressive Disorder or MDD) for which they are receiving treatment by a medical provider .

Take extra precaution and discuss with your clinician the following circumstances, if applicable:

- You are pregnant, think you might be, or become pregnant while using the device.
- You currently have thoughts about suicide or harming yourself.
- You have been told there is a problem with your skull or if you have metal parts in or around the brain, like brain surgery clips, metal plates or screws in the skull, cochlear implants or brain pacemakers such as those used for Parkinson's disease. It is fine to use the device if you have dentures.
- You have been diagnosed with "epilepsy", "seizure(s)", "seizure disorder", unexplained loss or alteration of consciousness, or according to a medical provider you have had symptoms of a possible seizure.
- You have a chronic skin condition affecting your forehead or scalp, such as psoriasis.

There is a risk that the device is ineffective for the individual patient. The device should only be used by patients whose clinical course is supervised by a medical provider.

7. Warnings

- Never change your treatment for depression (major depressive disorder) prior to discussing with your medical provider.
- The headset should never be applied to open wounds, damaged or irritated skin. If the skin is irritated, red or abnormal in any way since the device was last used, wait for the skin to heal completely before using the device.
- New headset pads should be used each time and these pads should not be dry.
- Never use tap water to wet pads.
- Apply the headset only on the head as directed. Do not apply the headset anywhere except the head.

- When using the device, avoid activities which may cause the headset to move or change position.

- Keep the headset dry.
- Keep the headset out of the reach of children.
- The headset should not be used around strong magnetic fields, e.g. near an MRI machine.

8. Possible Adverse Reactions

- Some skin redness under the electrode or near the electrode sites is normal due to increased local blood flow. The redness will normally subside within approximately an hour after the end of use.

- DO NOT apply the device over open wounds, or damaged or irritated skin. This might create further irritation and/or skin damage.

- Skin irritation might be experienced beneath the stimulation electrodes. In this case, electrodes should NOT be reapplied to the irritated skin. If you experience any dryness of the skin/skin irritation after stimulation, it is recommended to apply moisturizer to the area.

- Discontinue treatment if the sensation of tingling, itching or burning under electrodes becomes severe (mild sensations of tingling, itching or burning are normal).

- Discontinue treatment if you experience persistent or worsening headaches.

- Discontinue treatment if you experience persistent tinnitus (noise or ringing in the ears) during or after using the device.

If you have questions about adverse reactions, please talk with your medical provider or contact Flow Neuroscience.

NOTE: Any serious incident that has occurred in relation to use of the device should be reported to Flow Neuroscience (see section 18) and the FDA (see section 19).

9. The Treatment Program

- The Flow treatment program consists of 15 sessions during the first 3 weeks, as shown in the table below (W1, W2, and W3).
- After this first treatment period, up to 3 sessions are recommended per week (W4, W5+).
- The number of sessions you can do per week is restricted and you can only do 1 per day.
- Talk with your medical provider if you want to make changes to your stimulation schedule.
- Each session lasts 30 minutes, plus a few minutes of preparation time.

WEEK	W1	W2	W3	W4	W5+
No. of Sessions	5	5	5	1-3	1-3

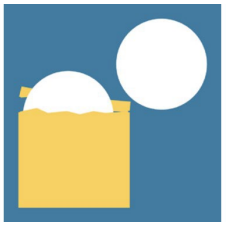
10. First-Time Use

- Download the “Flow - Depression treatment” app to your mobile device.
- Create an account in the downloaded “Flow - Depression treatment” app using an email address you have access to and a new password of your choosing.
- If a card with an activation code is supplied in the box, you might need to enter it in the app before your first session.

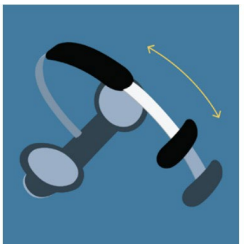
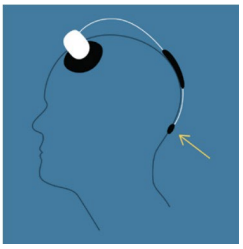
11. How to Perform a Treatment Session

- Ensure your forehead is free from any makeup or hair products before you start. Not doing so can result in skin damage.
- If you have a fringe, it is recommended that you use a hair tie to remove it from your forehead.
- Take out the headset from the box.
- Press the button on the headset and make sure the LED indicator starts blinking. If not, charge the headset.
- Make sure Bluetooth is enabled on your smartphone.

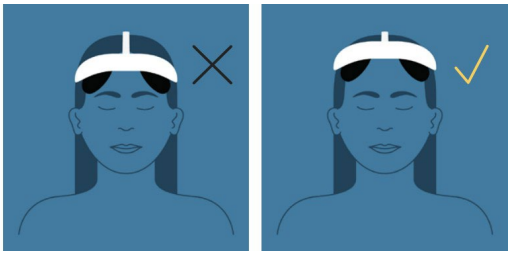
- Start the Flow app and log in with the email address & password you chose in Section 11 above.
- Follow the instructions in the app to start the stimulation.
- When told to, follow the instructions on how to prepare the headset, as below:
    - 1. Take a new pair of Headset Pads from their sachet. Reuse of pads can lead to skin damage.
    - 2. Attach them to the electrodes using the Pad Holder Rings.

1. 
2. 

    - 3. Adjust the length of the metal arch by sliding the back piece.
    - 4. The end of the arch should sit comfortably on the back of your head. Make sure the headset does not sit too low.

3. 
4. 

    - 5. The app shows you how to correctly position the headset using the camera on your device.

5. 

    - 6. Before starting the stimulation, you can press and hold the “Tingle” button in the app to test how the stimulation feels. Hold the “Tingle” button for at least 10 seconds.
    - 7. Start the stimulation by pressing the “Start stimulation” button in the app.

- The current will now slowly increase to its maximum of 2 mA, as shown in the app.

- If at any point you want to pause the stimulation, press the pause button in the app or the button on the headset.
- Follow the instructions in the app during the rest of the session. The session will last for 30 minutes.
- When the time is up, the headset will automatically start decreasing the current.
    - Do not remove the headset before the app indicates that the stimulation has stopped.
    - The headset gives a “beep” signal when the stimulation has finished.
    - After the session, dispose of the Headset Pads and put the Pad Holder Rings and headset back in the box.
- The headset will automatically turn itself off after a few minutes of inactivity. Start it again by pressing the button on the headset.

12. Charging the Headset

- Charge the headset if the LED indicator on the front of the headset does not blink when pressing the button.
- Remove the charger port cover and charge using the supplied Micro-USB charger and cable.
- The LED indicator blinks during charging and shows a steady light when the headset is fully charged.
- Recharging a fully flat battery takes approximately an hour.
- Be sure to close the charger port cover again after charging.

13. Cleaning of the Headset

- It is recommended to clean the headset and especially the electrodes after each use.
- To clean the device, ensure that the Micro-USB cable is not connected to the headset and remove the pads.
- Use an IPA (isopropanol) wet wipe (45% is a good choice).

- Clean the electrodes using a gentle circular motion.
- Neither the device nor its accessories are supplied sterilized nor require sterilization prior to use.

14. Clinical data

Pivotal study

The Flow FL-100 device was studied in a fully remote, two-site (UK, US), double-blind, placebo-controlled, randomized superiority trial of home-based treatment in patients diagnosed with major depressive disorder (MDD). Participants were adults 18 years or older who:

- were in a current depressive episode of at least moderate severity (based on a score ≥ 16 on the 17-item Hamilton Depression Rating Scale (HDRS-17);
- were not currently being treated for MDD, or had been receiving a stable dose of antidepressant medication or a stable schedule of psychotherapy for at least 6 weeks prior to study enrollment; and agreed to maintain the same treatment regimens throughout the trial.

The pivotal study included 2 parts (phases), each lasting 10 weeks:

1. Blinded phase: 50% of participants received active treatment with Flow FL-100 and 50% received inactive (placebo) treatment; treatment schedule – 5 sessions per week for 3 weeks then 3 sessions per week for 7 weeks.
2. Open-label phase: offered to persons who completed the Blinded phase; all participants received active treatment (Flow FL-100.

Active stimulation was 2 mA. The placebo (sham) stimulation, using the same device, was an initial current ramp up to 1 mA over 30 seconds then ramp down over 15 seconds and repeated at session end to provide a tingling sensation which mimics active stimulation.

Primary outcome in the Blinded phase was the between-group difference in mean HDRS-17 change at Week 10.

Results: 174 participants were randomized: active (n=87; mean age 37.1 + 11.1 years) and sham (n=87; mean age 38.3 + 10.9 years) treatment, with no differences in discontinuation rates between active (n=13) and sham (n=12). 63% were women.

Active treatment arm showed a statistically significant improvement in HDRS-17 from baseline to Week 10. Mean improvement was 9.4 points relative to 7.1 points for the sham treatment (delta: 2.3, 95% CI: 0.5 to 4.0, p = 0.012). Based on HDRS-17 ratings, active treatment arm showed a statistically significant greater clinical response rate of 54.4% relative to sham 26.9% (p = 0.001), Odds Ratio (OR): 3.25 (95% CI: 1.57 to 6.74), and the active treatment arm showed statistically significant greater remission rate of 44.9% relative to sham 21.8% (p = 0.004), OR: 2.93 (95% CI: 1.41 to 6.09).

Based on MADRS ratings, the active treatment arm showed a statistically significant improvement from baseline to Week 10. Mean improvement was 11.3 points relative to 7.7 points for the sham treatment (delta: 3.6, 95% CL: 1.1 to 6.1, p = 0.006). In clinical response, the active treatment arm showed a statistically significant greater response of 63.0% relative to sham 31.6% (p < 0.001), OR: 3.70 (95% CI: 1.82 to 7.52). In clinical remission, the active treatment arm showed a statistically significant greater remission rate 57.5% relative to sham 29.4% (p = 0.002), OR: 3.26 (95% CI: 1.53 to 6.94).

FL-100 was studied as both a monotherapy (without any antidepressants or psychotherapy) and as an adjunctive therapy. In the monotherapy group, results were as follows, based on HDRS-17:

- Number of participants who completed week 10 (Active vs Sham): 23 vs 29
- Mean score decrease: 9.74 vs 5.93, delta: 3.8, p=0.0027
- Response rate: 47.8% vs 13.8%, OR: 5.76, p<0.0001
- Remission rate: 34.8% vs 13.8%, OR: 3.29, p=0.0027

Safety: Flow FL-100 was well-tolerated in all subjects and there were no serious adverse events (SAEs) associated with use of the device. At Week 10, there were increased reports of skin redness (p < 0.001), skin irritation (difference 6.9% (1.9% to 14.5%) p = 0.03) and trouble concentrating during stimulation (p = 0.03) in active relative to sham, and no differences in headache, neck pain, scalp pain, itching, burning sensation, sleepiness, tinnitus, or acute mood changes between treatment arms was observed.

15. Device Specifications

PERFORMANCE CHARACTERISTICS	
PARAMETER	**NOMINAL VALUE**
MAX. STIMULATION CURRENT	2.0 ± 0.05 mA
MAX. STIMULATION VOLTAGE	24 V
MICRO-USB CHARGER	5 V D.C.
BATTERY	RECHARGEABLE LiPo 3.7 V; 250 mAh
ELECTRODE SIZE	22.9 cm2 (5.4 cm diameter)
DEVICE WEIGHT	~110 g
WATER INGRESS PROTECTION	IP22
DEVICE EXPECTED LIFETIME	3 YEARS
OPERATING ENVIRONMENT	HOME OR CLINICAL ENVIRONMENT
OPERATING TEMP. RANGE	5 to 35°C (41 to 95°F)
STORAGE/TRANSPORT TEMP. RANGE	-10 to 40°C (14 to 104°F)
OPERATING HUMIDITY RANGE	10% to 93%, NON-CONDENSING

STORAGE/TRANSPORT HUMIDITY RANGE	10% to 93%, NON-CONDENSING

OPERATING ALTITUDE RANGE	0–3000 m
STORAGE/TRANSPORT ALTITUDE RANGE	0–3000 m

The Bluetooth connection uses a non-secure mode where a device will not initiate security procedures and authentication and encryption are bypassed.

16. Markings

ICON	DEFINITION
	Consult Instruction for Use (IFU)
	Caution: Consult Accompanying Documentation
	Separate collection for electrical and electronic equipment per EC Directive 2012/19/EU. Waste Electrical and Electronic Equipment (WEEE).
	Type BF Applied part
	Manufacturing Year
	Keep Dry
	Manufactured by Flow Neuroscience AB Södra Tullgatan 3, 211 40 Malmö, Sweden, Web: flowneuroscience.com
IP22	Water ingress protection: 22
	Bluetooth Low Energy
	Prescription use only

17. Product Disposal

- Headset Pads are cellulose sponges and can safely be disposed of as household waste.
- The headset and charger should be disposed of as electronic waste according to the local legislation.

18. Contact Us

If you have any questions regarding Flow, don't hesitate to contact customer support at https://www.flowneuroscience.com/support/

NOTE: Any serious incident that has occurred in relation to the device should be reported to Flow Neuroscience and the FDA (see section 19).

19. Reporting adverse events

MedWatch is the Food and Drug Administration's (FDA) program for reporting serious reactions, product quality problems, therapeutic inequivalence/failure, and product use errors with human medical products, including drugs, biologic products, medical devices, dietary supplements, infant formula, and cosmetics.

If you think you or someone in your family has experienced a serious reaction to a medical product, you are encouraged to take the reporting form to your doctor. Your health care provider can provide clinical information based on your medical record that can help FDA evaluate your report.

However, we understand that for a variety of reasons, you may not wish to have the form filled out by your healthcare provider, or your healthcare provider may choose not to complete the form. Your health care provider is not required to report the information. In these situations, you may complete the Online Reporting Form yourself.

You will receive an acknowledgement from the FDA when your report is received. Reports are reviewed by FDA staff. You will be personally contacted only if we need additional information.

Submitting Adverse Event Reports to FDA

Use one of the methods below to submit voluntary adverse event reports to the FDA:

- Report Online at www.accessdata.fda.gov/scripts/medwatch/index.cfm?action=reporting.home

- Consumer Reporting Form FDA 3500B. Follow the instructions on the form to either fax or mail it in for submission. For help filling out the form, see MedWatchLearn. The form is available at www.fda.gov/downloads/aboutFDA/reportsmanualsforms/forms/ucm349464.pdf

- Call FDA at 1-800-FDA-1088 to report by telephone.

- Reporting Form FDA 3500 is commonly used by health professionals. The form is available at www.fda.gov/downloads/aboutFDA/reportmanualsforms/forms/ucm163919.pdf

20. EMC - Test Results

The device does not emit any radiation intended for medical purposes, neither hazardous nor potentially hazardous radiation.

EMISSION LIMITS & MEASUREMENT				
PHENOMENON	**STANDARD**	**TEST METHOD**	**TEST LEVELS**	**RESULT**
RADIATED RF EMISSION	IEC 60601-1-2	CISPR 11 ETSI EN 301 489-1	30~1000 MHz ; 1~3 GHz & 3~6 GHz (Measurement Uncertainty 4.24 dB)	PASS
CONDUCTED RF EMISSION	IEC 60601-1-2	CISPR 11 ETSI EN 301 489-1	0,15~30 MHz (Measurement Uncertainty 3.35 dB)	PASS
VOLTAGE FLUCTUATION & FLICKER	IEC 60601-1-2	IEC 61000-3-3	**EUT VALUES & LIMITS** Pst: 0.028 ; Limit 1.00 Plt: 0.028 ; Limit 0.65 dc [%]: 0.0000 ; Limit 3.30 dmax [%]: 0.053 ; Limit 4.00 dt [s]: 0.000 ; Limit 0.50	PASS

IMMUNITY LIMITS & MEASUREMENT				
PHENOMENON	**STANDARD**	**TEST METHOD**	**TEST LEVELS**	**RESULT**
ELECTROSTATIC DISCHARGE	IEC 60601-1-2	IEC 61000-4-2	±2 kV, ±4 kV, ± 6 kV, ± 8 kV - Contact Discharge ± 2 kV, ± 4 kV, ± 8 kV, ± 15 kV - Air Discharge	PASS
RF ELECTROMAGNETIC FIELDS	IEC 60601-1-2	IEC 61000-4-3	10 V/m 80 – 2700 MHz 80 % AM at 1 kHz	PASS
ELECTRICAL FAST TRANSIENTS COMMON MODE / BURSTS	IEC 60601-1-2	IEC 61000-4-4	± 2 kV for A.C. Power Lines 100 kHz Burst Frequency	PASS
SURGES LINE TO LINE	IEC 60601-1-2	IEC 61000-4-5	± 0.5 kV & ±1 kV At 0°, 90°, 180°, 270° ; Repetition Rate: 60 S	PASS
SURGES LINE TO GROUND	IEC 60601-1-2	IEC 61000-4-5	± 0.5 kV, ±1 & ±2 kV At 0°, 90°, 180°, 270°	PASS
RF COMMON MODE	IEC 60601-1-2	IEC 61000-4-6	3 & 6 V for A.C. Main Port ; 80%, 1 kHz Amplitude Modulation) Frequency: 150kHz to 80MHz	PASS

VOLTAGE DIPS & INTERRUPTIONS	IEC 60601-1-2	IEC 61000-4-11	0 % UT; 0,5 Cycle At 0°, 45°,90°, 135°,180°, 225°, 270°, 315°, 0 % UT; 1.0 Cycle 70 % UT; 25/30 Cycles	PASS

END OF THE CORE TEXT