Argus® II
Retinal Prosthesis System

Product Insert

Rx Only: Federal law restricts this device to sale by or on the order of a physician.

HUMANITARIAN DEVICE: Authorized by Federal (U.S.) law to provide electrical stimulation of the retina to induce visual perception in blind patients with severe to profound retinitis pigmentosa and bare light or no light perception in both eyes. The effectiveness of this device for this use has not been demonstrated.

900007-003 Rev D

Argus® II
Retinal Prosthesis System

Product Insert

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DEVICE DESCRIPTION

The Argus II Retinal Prosthesis System (hereinafter referred to as "Argus II System") consists of implanted and external components. The implant is an epiretinal prosthesis that includes a receiver, electronics, and an electrode array that are surgically implanted in and around the eye. The array has 60 electrodes arranged in a rectangular grid, of which 55 are enabled. It is attached to the retina over the macula with a retinal tack. The external equipment includes glasses, a video processing unit (VPU) and a cable. The glasses include a miniature video camera, which captures video images, and a coil that transmits data and stimulation commands to the implant. The VPU converts the video images into stimulation commands and is body-worn. The cable connects the glasses to the VPU. The Argus II System operates by converting video images into electrical energy that activates retinal cells, delivering the signal through the optic nerve to the brain where it is perceived as light. The Argus II Clinician Fitting System (CFS) and Psychophysical Test System (PTS) are used in the clinic to test and program the Argus II Implant and External Equipment.

INDICATIONS FOR USE

The Argus II Retinal Prosthesis System is intended to provide electrical stimulation of the retina to induce visual perception in blind patients. It is indicated for use in patients with severe to profound retinitis pigmentosa who meet the following criteria:

- Adults, age 25 years or older.
- Bare light or no light perception in both eyes. (If the patient has no residual light perception, then evidence of intact inner layer retina function must be confirmed.)
- Previous history of useful form vision.
- Aphakic or pseudophakic. (If the patient is phakic prior to implant, the natural lens will be removed during the implant procedure.)
- Patients who are willing and able to receive the recommended post-implant clinical follow-up, device fitting, and visual rehabilitation.

The Argus II implant is intended to be implanted in a single eye, typically the worse-seeing eye.

CONTRAINDICATIONS

- Ocular diseases or conditions that could prevent the Argus II System from working (e.g. optic nerve disease, central retinal artery or vein occlusion, history of retinal detachment, trauma, severe strabismus, etc.).

- Ocular structures or conditions that could prevent the successful implantation of the Argus II Implant or adequate healing from surgery (e.g. extremely thin conjunctiva, axial length <20.5 mm or >26 mm, corneal ulcers, etc.).
- Ocular diseases or conditions (other than cataracts) that prevent adequate visualization of the inner structures of the eye (e.g. corneal opacity, etc.).
- Inability to tolerate general anesthesia or the recommended antibiotic and steroid regimen associated with the implantation surgery.
- Metallic or active implantable device(s) (e.g. cochlear implant) in the head.
- Any disease or condition (e.g. significant cognitive decline, etc.) that prevents understanding or communication of informed consent, fitting of the Argus II System, or post-operative follow-up. A pre-operative psychological evaluation may be recommended to confirm the patient is not contraindicated based on this criterion.
- Predisposition to eye rubbing.

WARNINGS

- Failure to **follow the recommended surgical procedure** for implanting the Argus II Implant may increase the risk of adverse events and damage to the implant.
- **Individuals implanted with an Argus II Implant should not undergo short wave or microwave diathermy**. High currents induced in the implant electrodes can cause tissue damage or serious injury. Diathermy may also cause permanent damage to the implant.
- **Individuals implanted with an Argus II Implant should not undergo electroconvulsive therapy (ECT)** as ECT may cause tissue damage or permanent damage to the implant.
- If **lithotripsy or high output ultrasound** must be used, do not focus the treatment beam near the Argus II Implant. Exposure of the Argus II Implant to these therapies may harm the patient or damage the implant.
- The Argus II Implant has been classified as an **MR Conditional** device. Individuals with an Argus II Implant may undergo a **magnetic resonance imaging (MRI)** procedure ONLY if it is performed using a 1.5 or 3.0 Tesla MRI System and ONLY following the MRI Instructions provided later in this insert. Individuals with an Argus II Implant should not enter a room housing an MRI System that has a rating other than 1.5 or 3.0 Tesla, even if the Argus II System is not being used. The external equipment (i.e. VPU and glasses) should remain outside

the MR system room, as **severe harm to people in the MR system room could occur.** If any pain is experienced during the MRI procedure the patient should be instructed to notify the technician immediately.

- The Argus II System may interfere with the operation or accuracy of **medical monitoring, diagnostic or life support equipment.** Do not use the Argus II System within 3 feet (0.9 meters) of this type of equipment. If interference occurs, turn off the Argus II VPU or extend the distance between yourself and the affected equipment.
- Do not use **monopolar electrosurgical equipment** in individuals with an Argus II Implant. Monopolar electrosurgical equipment may cause damage to the implant or to tissue surrounding the implant.

PRECAUTIONS

- In the event of any **undesirable sensation** when using the Argus II System (for example, pain), immediately halt operation of the system by removing the Argus II Glasses or turning off the Argus II VPU.
- At any time after implantation, Argus II patients have a risk of conjunctival complications which, if left untreated, may result in conjunctival erosion which could lead to endophthalmitis. Argus II recipients should be vigilant in reporting any new symptoms of foreign body sensations, tearing and/or pain promptly to their eye care professional. Long-term professional monitoring for late conjunctival issues is necessary.
- The long-term effects of **chronic electrical stimulation** are unknown. Such effects may include deterioration of the retina or optic nerve. These effects may lead to deterioration of residual native vision and/or visual response to the Argus II System and could preclude subsequent replacement of the Argus II Implant with another retinal implant.
- Individuals with an Argus II Implant should **only use a VPU that has been specifically programmed for them** by their clinician or Second Sight personnel. Use of a different VPU may be ineffective in providing visual information and may cause physical discomfort from overstimulation.
- To avoid unsafe stimulation, do not use a **VPU configured for Operating Room** use for anything other than pre-implantation testing, testing during implantation, or initial fitting testing.
- Individuals with an Argus II Implant should **avoid physical impact or extreme direct pressure to the eye** as this

may result in eye trauma, movement or damage to the Argus II Implant. If this occurs, consult your physician.

- Individuals with an Argus II Implant should **avoid eye rubbing** as this may dislodge the implant or cause eye irritation.
- Individuals with an Argus II Implant should continue to use their other **mobility aids** (e.g. canes, dogs, etc.) at all times.
- Use of the Argus II System during **pregnancy and nursing** has not been evaluated.

Precautions Regarding Other Medical Procedures

General Information (applicable to all procedures)

- Individuals needing to undergo any of the procedures listed below, should inform his or her doctor about the existence of a retinal prosthesis in the eye. The doctor should contact Second Sight at 1-818-833-5060 for more information.
- **Before having any medical or test procedure that involves the use of other medical equipment, individuals with an Argus II Implant should remove the Argus II Glasses and VPU.**
- Once the procedure is complete, that individual should have the Argus II Implant tested as soon as possible to make sure it is still functioning properly. Damage to the implant may not be immediately detectable.

Information about Specific Procedures

- **Magnetic Resonance Imaging (MRI)** – Refer to the Warnings section above and the MRI Information section below for more information about MRI.
- The use of **laser, phacoemulsification, or fragmatome** may damage the Argus II Implant. If these procedures must be used in an implanted eye, do not direct the laser beam at the implant. Extra caution should be used when performing these procedures intraocularly as visualization of the implant may be obscured.
- The use of **bipolar electrosurgical equipment** may damage the Argus II Implant. Use caution when using this equipment near the implant.
- **CT Scans or Diagnostic Ultrasound** may be performed in individuals with an Argus II Implant. However, if a scan or ultrasound is performed in the region where the Argus II

Implant is located, the implant may create an image artifact making the scan unreadable in this region.

- Use of **defibrillators or therapeutic ionizing radiation to the head** may permanently damage the Argus II Implant. However, this should not preclude or change the way in which these treatments are delivered. The Argus II Implant should be tested by a qualified clinician or Second Sight personnel as soon as possible following the procedure or defibrillator activation to confirm that it is still functioning properly. Damage to the implant may not be immediately detectable.
- The effects of **cobalt treatment and linear acceleration** techniques on the implant are unknown.

Electromagnetic Interference (EMI)

Electromagnetic interference is a field of energy (electrical, magnetic, or both) created by equipment found in public environments that may be strong enough to interfere with the normal operation of the Argus II System. The Argus II System meets international standards for electromagnetic compatibility and is designed to continue to operate in a "safe mode" in the presence of any electromagnetic interference which would normally be encountered during every day use of the Argus II System. It is important to note, however, that in certain circumstances, electromagnetic interference could cause the following:

- **Serious injury.** Exposure of the implant to EMI may result in the implant heating and damaging nearby retinal tissue. See "Warnings" on page 2.
- **Damage to the Argus II implant.** Damage to the implant may require replacement, or result in loss of, or irreversible change in the performance of the Argus II System. See "Warnings" on page 2.
- **Unexpected Turning off of the Argus II VPU.** EMI may cause the VPU to turn off unexpectedly.
- **Interruption of Stimulation.** EMI may cause a momentary interruption of stimulation.

Argus II System users should be advised that upon entering an environment which maybe causing interference with the Argus II System, they should move away from the equipment or object thought to be causing the interference, if possible, turn off the equipment or object causing the interference, tell the equipment operator or the doctor what happened and, if they continue to

experience interference or think that the Argus II System is not working as well as it did before they encountered the interference, to contact their doctor.

Information to User (FCC Rules)

This device complies with Part 15 of the FCC Rules. Operation is subject to the following two conditions: (1) This device may not cause harmful interference, and (2) This device must accept any interference received, including interference that may cause undesired operation.

This equipment has been tested and found to comply with the limits for Class B Digital Device, pursuant to Part 15 of the FCC Rules. These limits are designed to provide reasonable protection against harmful interference in a residential installation. This equipment generates and can radiate radio frequency energy and, if not installed and used in accordance with the instructions, may cause harmful interference to radio communications. However, there is no guarantee that interference will not occur in a particular installation. If this equipment does cause harmful interference to radio or television reception, which can be determined by turning the equipment off and on, the user is encouraged to try to correct the interference by one or more of the following measures.

- Reorient or relocate the receiving antenna
- Increase the separation between the equipment and receiver
- Connect the equipment into an outlet on a circuit different from that to which the receiver is connected
- Consult the dealer or an experienced radio/TV technician for help

Any changes or modifications not expressly approved by Second Sight Medical Products, Inc. could void the user's authority to operate the equipment.

Possible Interference with Other Electronic Devices

- **Theft or metal detectors** (such as those located in entrances to public buildings and department stores) and **airport or security screening devices** may temporarily interrupt Argus II stimulation if the Argus II System is used within 1 yard (0.9 meters) of them. Normal operation will resume when you move away from these items. When

possible, it is best to avoid these devices or turn the VPU off when passing through these systems. Individuals with an Argus II Implant should show their ID card to any attendant in the area who may be able to assist them in bypassing the devices. If unavoidable, walk through the scanner and promptly move away from the area. Do not lean on these scanners or linger in their path.

- **Electronic Article Surveillance (EAS) systems, EAS Tag Deactivators, and Radiofrequency identification (RFID) systems** may temporarily interrupt Argus II stimulation if the Argus II System is used within 3.5 yards (3.2 meters) of them. Normal operation will resume when you move away from these items. RFID systems and EAS systems and tag deactivators send out energy fields that wirelessly communicate with tags that are attached to objects such as merchandise, materials and people. These systems are used for security, theft prevention, tracking and inventory control and they are usually found in retail stores, libraries, government buildings, warehouses and offices. For example, security tags attached to clothing contain RFID tags.
- **Electrostatic Discharge (ESD)** may interfere with normal operation or cause damage to the electrical components of the Argus II System. Common situations that create static electricity include putting on or removing clothes, or dragging feet across a carpet or rug when there is less than 30% relative humidity. Care should be taken to avoid handling the VPU and glasses when static electricity is present.
- The Argus II System may interfere with the normal operation of some models of **hearing aids**. Hearing aids should be tested prior to implantation, to ensure proper functioning of both the Argus II System and the hearing device.
- Some **home appliances** (for example, microwaves) and some **devices with antennae** (for example, cell phones, and cordless phones) may temporarily interrupt Argus II stimulation if the Argus II System is being used near them. The table below lists the distance at which interruption of stimulation may occur with these systems.

Table 1: Separation Distances

Type of device	Interruption of stimulation may occur if device is operated within this distance of the Argus II System
Another Argus II System	7 inches (17.5 cm)
Cell phone	1 inch (2.5 cm)
Cordless phone	1 inch (2.5 cm)
Bluetooth device	1 inch (2.5 cm)
Microwave oven	1 inch (2.5 cm)
WiFi Access Point	8 inches (20 cm)
Wireless Router	8 inches (20 cm)

Normal operation will resume when you move away from these items.

- The Argus II System operates using wireless technology which could interfere with the safe operation of an **airplane**. Patients should not turn on the Argus II System on an airplane.
- **Commercial electrical equipment** (such as arc welders, induction furnaces or resistance welders), **communication equipment** (such as microwave transmitters, linear power amplifiers and high-power amateur transmitters**), high voltage lines, power lines or generators, electric steel furnaces, or large magnetized speakers** may temporarily interrupt Argus II System function. Normal operation will resume when you move away from these items.

For additional information on specific environments and recommended separation distances please see the tables provided in the Electromagnetic Environments section of this insert.

Air Travel, General Travel and International Use

CAUTION: **The Argus II System operates using wireless technologies that could interfere with the safe operation of an airplane and should not be turned on or used on an airplane.**

When travelling and not using the Argus II System, individuals should be advised to store the external equipment in the travel case. International travel may require the use of adapters to be able to plug the VPU battery charger into an electrical outlet. Individuals

with the Argus II System should be advised to both bring their patient identification card with them to assist in going through security systems and to turn off the VPU. If individuals with the Argus II System are experiencing any medical complications before traveling, they should be advised to speak with a doctor to determine if it is safe for them to travel, especially on a plane. They also may wish to obtain the name of a local ophthalmologist, in the event of any complications during their travels.

Precautions in the Event of Change in Device Performance

If there is a notable change in performance with the Argus II System, the patient should contact his or her clinician for assistance. A visit to the clinic for troubleshooting, diagnostic tests, or re-programming may be required.

CLINICAL CONSIDERATIONS

- The Argus II System is not intended to slow or reverse the progression of the disease.
- The Argus II System provides “artificial” vision; it does not restore normal vision.
- The Argus II Implant is intended to be implanted in a single eye. In general, the Argus II Implant should be implanted in the worse-seeing eye. If both eyes have equivalent residual vision and are equally suitable for implantation, the patient’s preference for the implanted eye should be respected.
- The Argus II Implant is made specifically for either the left eye or the right eye. Before opening the Argus II Implant package, carefully read the label and verify that the package contains the desired device.
- Abnormalities in the typical curvature of the retina (e.g. staphyloma), especially significant protrusions or depressions in the area centralis, could affect how well the Argus II Implant fits against the retina. If the implant does not fit well against the retina, the patient’s performance with the device may not be optimal.
- It is strongly recommended that a preoperative psychosocial evaluation be performed to determine a patient’s level of motivation, expectations of the device, ability to deal with potentially disappointing results, and the extent of their social support network.
- The patient should have the cognitive and physical ability to operate the Argus II VPU and glasses.

- If the patient is severely hearing impaired, prior to implantation the clinician should test to see if the patient can hear the VPU's audible alerts using a hearing aid or other assistive listening devices. If the patient cannot hear these audible alerts when aided, the clinician should confirm that the patient has someone who can assist them in hearing and understanding these alerts. In addition, the clinician should be able to adequately communicate with the patient in order to program the Argus II System.
- Based on the spacing of the electrodes, the theoretical limit of resolution of the Argus II is 2.1 logMAR. However, in the clinical trial, one subject achieved a resolution better than this (i.e. 1.8 logMAR), likely due to head scanning.
- Each Argus II implant has 60 electrodes, of which 55 are enabled. Up to 5 of the remaining electrodes may be functional and could be enabled to replace an electrode if it fails post-implant.
- Patients should live within a distance (or be willing to temporarily relocate to a distance) that will allow their full participation in recommended post-operative clinical follow-up, device fitting and training, and visual rehabilitation.

REPORTED ADVERSE EVENTS

A total of 30 subjects were implanted with Argus II in a clinical trial (14 were implanted in the United States and 16 were implanted in Europe). Follow-up time ranged from 2.6 to 4.8 years (average was 3.5 years). One subject's device was explanted at 1.2 years due to recurrent conjunctival erosion and refractory hypotony.

Definition of Adverse Events

In the study, serious adverse events (SAEs) were medical occurrences that:

- Necessitated medical or surgical intervention to preclude permanent impairment of a body function or permanent damage to a body structure; OR
- Caused permanent impairment of a body function or permanent damage to body structure; OR
- Required hospitalization or prolonged hospitalization.

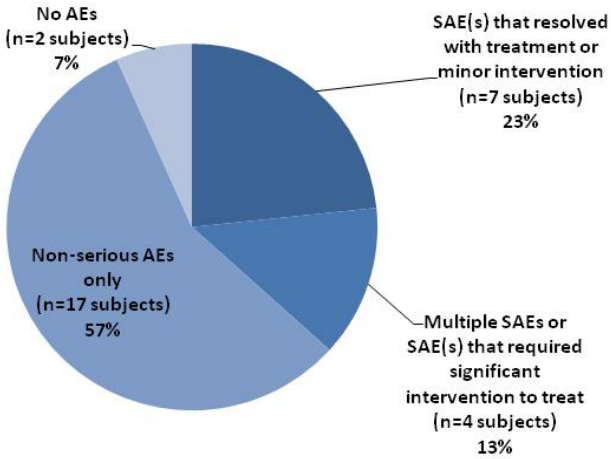
Events not meeting the above criteria were considered non-serious. All device-related or surgery-related events are summarized below.

Overview of Safety Experience

Nineteen (19) subjects (63%) experienced no, or only non-serious, adverse events. These non-serious events were treated routinely with medication or observation only. An additional 7 subjects experienced SAEs that resolved with treatment or minor interventions.

The remaining 4 subjects were distinct from the other subjects in that they had a higher rate of adverse events due to a cascade of related events. In total, these 4 subjects accounted for 57% of all serious adverse events (SAEs) and 24% of all non-serious adverse events. Refer to Figure 1.

Figure 1: Overview of Safety Experience (n=30 subjects)



Serious Adverse Events

Nineteen subjects did not have any device- or surgery-related serious adverse events (SAEs). Eleven subjects experienced a total of 23 device- or surgery-related SAEs (Refer to Table 2). Ten of the 23 events were considered to be related to the Argus II device and the remaining 13 were considered to be related to a surgical procedure. SAEs were generally treated with a surgical re-intervention, with the exception of endophthalmitis, keratitis, and uveitis which were treated with topical and/or intravitreal antibiotics. Infective corneal melt was treated with antibiotics, steroids and cross-linking.

Certain trends were observed in SAEs. First, the majority of SAEs occurred within the first few months post-implant (more than 60% occurred within the first 6 months and 35% occurred within the first 6 weeks). Second, SAEs tended to be clustered in a few subjects. Two subjects accounted for almost half of all SAEs (10/23). In these cases, the main event either required multiple interventions to treat it or the subject experienced a cascade of inter-related events.

Table 2: Serious Adverse Events (Device- or Surgery-Related)

Event	# of Subjects	# of Events	% Subjects (n=30)
Conjunctival dehiscence	3	3	10.0%
Conjunctival erosion	3	4	10.0%
Corneal Melt - infective	1	1	3.3%
Corneal Opacity	1	1	3.3%
Fibrotic events:	3	3	10.0%
RD - rhegmatogenous	1	1	3.3%
RD - tractional and serous	1	1	3.3%
Retinal Tear	1	1	3.3%
Hypotony	4	4	13.3%
Intraocular inflammatory events:	3	4	10.0%
Endophthalmitis - infective	3	3	10.0%
Uveitis	1	1	3.3%
Keratitis - infective	1	1	3.3%
Re-tack	2	2	6.7%

RD = retinal detachment

Non-Serious Adverse Events

Any adverse event that did not meet the definition of an SAE was considered to be a non-serious adverse event. These events normally resolved on their own or were treated with medical management (i.e. they did not require surgical re-intervention to treat). There were 140 non-serious device-or surgery-related adverse events (in 28 subjects), of which 78 were device-related and the remaining 62 were surgery-related. The following non-serious events were reported (number of events is indicated in parentheses): ocular pain (17), conjunctival congestion (11), epiretinal membrane (11), elective revision surgery (7), non-serious hypotony (7), suture irritation (7), choroidal detachment (6),

uveitis (6), inflammatory conjunctivitis (5), retinal thickening with cystoid macular edema (CME) (5), ocular inflammation (4), retinal thickening with no cystic changes (4), vitreous hemorrhage (4), headache (3), high intraocular pressure (3), hyphema (3), keratic precipitates (3), corneal vascularization (2), epiphora (lacrimation) (2), and foreign body sensation (2). There was one reported case of each of the following events: 360^{o} circumferential vitreous band traction, choroidal effusion, conjunctival cyst, conjunctival dehiscence, conjunctival erosion, corneal abrasion, corneal dryness, corneal epithelial defect, corneal filaments, corneal fold, corneal suture broken, decrease in light perception, fibrosis around the tack, filamentary keratitis, nausea, nystagmus increase, ocular fibrin, proliferative vitreo-retinopathy, ptosis, serous retinal detachment, tractional retinal detachment, retinal folds, retinoschisis, rubeosis, scleral patch displacement, scleritis, sub-conjunctival eyelashes, and vertigo.

Surgical Re-Interventions

Nine (9) subjects required a surgical re-intervention(s) to treat a device- or surgery-related adverse event(s). Seven (7) subjects had elective revision surgery. Refer to Table 3. In cases where it was necessary to remove all or part of the implant and/or tack (i.e. 1 case of explant and 3 cases where the retinal tack was removed to reposition the implant during an elective revision surgery), no adverse sequelae occurred.

Table 3: Surgical Re-Interventions

	# of Subjects	# of Events	% Subjects (n=30)
Re-intervention to treat an AE:	9	28	26.7%
Conjunctiva repair	5	12	16.7%
Corneal scraping with EDTA	1	1	3.3%
Device explant	1	1	3.3%
RD repair	2	4	6.7%
Re-tack	2	2	6.7%
Treatment of hypotony	2	4	6.7%
Laser - Retinal tear	2	3	6.7%
Cross linking for corneal melt	1	1	3.3%
Elective revision surgery	7	7	23.3%

RD = retinal detachment
EDTA = Ethylenediaminetetraacetic acid

POTENTIAL ADVERSE EVENTS

The following device-related or implant surgery- related adverse events were not observed during the clinical trial, but could potentially occur:

- Facial nerve stimulation, transient electrical shock, skin burn due to excessive heating of the external equipment, or retinal tissue damage due to mechanical trauma, excessive stimulation or excessive heating of the implant.
- Failure or damage to the Argus II Implant requiring it to be explanted.
- Fall or bump resulting from use of the Argus II System.
- Risks known to be associated with standard vitreo-retinal surgery, peeling of an epiretinal membrane and use of a scleral band: suprachoroidal hemorrhage, intrusion/extrusion of the scleral band, and macular hole.
- Risks known to be associated with the removal of the lens using clear cornea phacoemulsification: cortical drop in vitreous or vitreous prolapse.
- Risks known to be associated with canthotomy: improper apposition of the eyelids, chronic irritation at the lid margin.
- Risks known to be associated with the use of general anesthesia, steroids and antibiotics: chest pain, urinary retention, myocardial infarction, pulmonary embolism, deep vein thrombosis, respiratory failure, blood loss requiring transfusion, systemic infection, prolonged hospitalization, and allergic reaction to anesthesia.

PROBABLE BENEFIT

The Argus II System provided all 30 subjects with benefit as measured by visual function tests, although this level of benefit was variable. All 30 subjects were able to see visual percepts when the Argus II was electrically activated.

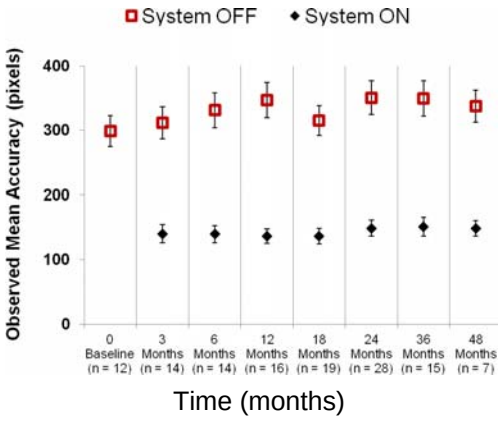
On the Square Localization test (i.e. object localization), subjects were consistently able to perform better with the System ON versus System OFF over the course of the study. Figure 2 displays the observed mean accuracy which indicates the subjects' mean distance from the center of the target square. Error bars represent the mean of the standard error.

On the Direction of Motion test, subjects were consistently able to perform better with the System ON versus System OFF over the course of the study. Figure 3 displays the observed mean accuracy which indicates the mean response error between the angle

displayed and the subject's response. Error bars represent the mean of the standard error.

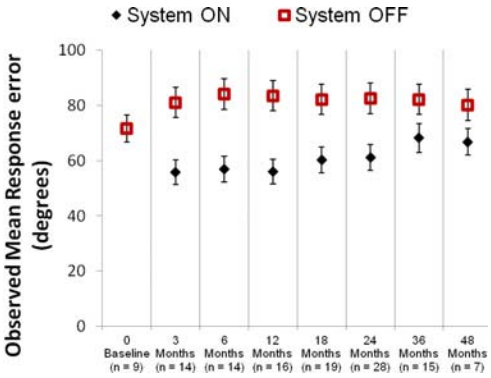
On the Grating Visual Acuity test, the most difficult of the 3 tests, 27% of subjects were able to reliably score on the scale (between 1.6 and 2.9 logMAR with a confidence interval within the scale) at least once with the System ON, while none of the Argus II subjects were ever able to score on the scale with the System OFF in either eye. (Table 4)

Figure 2: Square Localization Results



NOTE: Since this test was introduced midway through the study, the Baseline to 12-month results were only from subjects enrolled in 2009. Subjects enrolled in the study in 2007 and 2008 first performed this test at either their 18- or 24-month follow-up visit.

Figure 3: Direction of Motion Results



NOTE: Since this test was introduced midway through the study, the Baseline to 12 month results were only from subjects enrolled in 2009. Subjects enrolled in the study in 2007 and 2008 first performed this test at either their 18 or 24 month follow-up visit.

Table 4: Grating Visual Acuity (n=30)

	% of Subjects Whose Visual Acuity Improved to Less Than 2.9 LogMAR*
System ON	27% (n=8)
System OFF Implanted Eye	0% (n=0)
System OFF Fellow Eye	0% (n=0)

* Best result at any follow-up visit.

The Argus II System was also able to provide subjects with benefit as measured by objectively-scored, partially-controlled functional vision tests. Subjects consistently performed better with the Argus II System ON vs. OFF on orientation and mobility tests (finding a door and following a line, Figure 4 and Figure 5, respectively).

Figure 4: Door Task Results

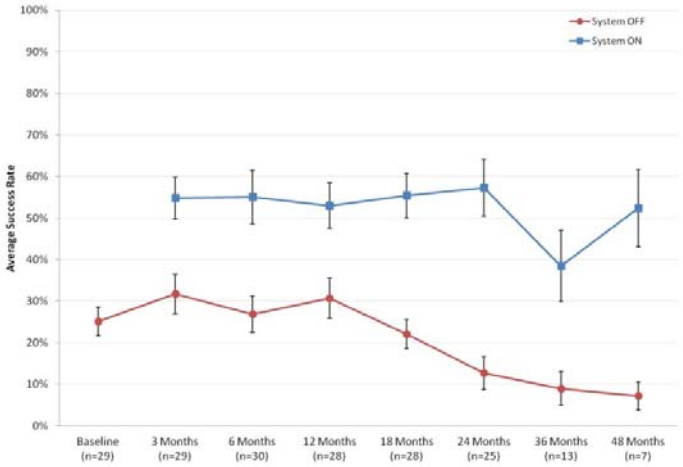
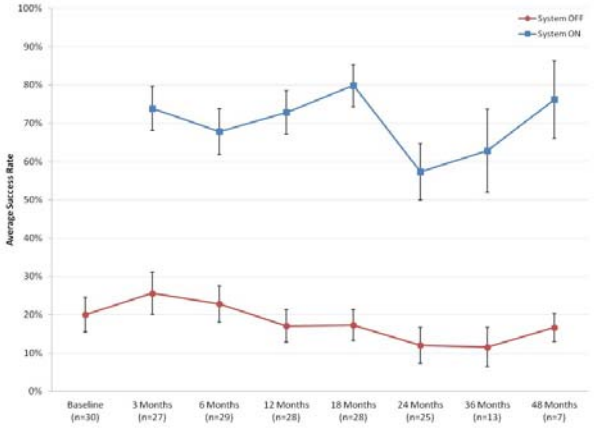


Figure 5: Line Task Results



Self-report questionnaires of activities of daily living and quality of life indicated mild improvement (Massof Activity Inventory) or no change (VisQOL), respectively.

An assessment of Argus II subjects in and around their home by independent, certified low vision rehabilitation specialists was also performed. This assessment, called the Functional Low-vision

Observer Rated Assessment (FLORA) was designed to evaluate how the Argus II System affected subjects' well-being and functional vision. It was added to the study in 2010 at which time subjects' length of follow-up ranged from 1.4 to 3.7 years post-implant. In no cases did the assessors report that the Argus II System had a negative impact on subjects. In 77% of cases, assessors using the FLORA determined that the subject was receiving (or had received at one time) functional vision and/or well-being benefit from the Argus II System. Refer to Table 5.

Table 5: Summary of FLORA Results (n=26 subjects)

Effect	Number of Subjects
Positive	9 (35%)
Mild Positive	7 (27%)
Prior Positive	4 (15%)
Neutral	6 (23%)
Negative	0 (0%)

Note: 4 subjects did not participate in the FLORA.

Implant Failures

One Argus II Implant experienced an intermittent communication link beginning at 10 months post-implant which led to a significant decline in the functionality of the device.

This device eventually failed approximately 4 years post-implant; however, the device remained implanted.

MRI INFORMATION

The Argus II Implant is MR Conditional according to the terminology specified in the American Society for Testing and Materials (ASTM) International, Designation: F2503-08, Standard Practice for Marking Medical Devices and Other Items for Safety in the Magnetic Resonance Environment. Non-clinical testing demonstrated that the Argus II Implant meets the MR Conditional classification.

WARNING 

Do NOT take the Argus II VPU or glasses into the MR system room. <u>The VPU and glasses are MR Unsafe.</u> The VPU and glasses were not tested in the MRI environment and are not permitted to be worn by the patient in the MR system room. Severe harm to the patient and/or damage to the external equipment may occur.

An individual with an Argus II Implant may safely undergo an MRI procedure under the conditions specified below:

- Static magnetic field of 1.5 Tesla or 3.0 Tesla
- Maximum spatial gradient magnetic field of 720-Gauss/cm or less
- Maximum MR system reported, whole body averaged specific absorption rate (SAR) of 2-W/kg for 15 minutes of scanning (i.e. per pulse sequence)
- Normal Operating Mode of operation for the MR system

MRI-Related Heating, 1.5-Tesla

In non-clinical testing, the Argus II Implant produced the following temperature rise during MRI performed for 15-min of scanning (i.e., per pulse sequence) in the 1.5-Tesla (1.5-Tesla/64-MHz, Symphony, Siemens Medical Solutions, Erlangen, Germany) MR system: Highest temperature change was +0.6˚C.

Therefore, the MRI-related heating for the Argus II Implant at 1.5-Tesla using a transmit/receive RF body coil at an MR system reported whole body averaged SAR of 3.5-W/kg indicated that the greatest amount of heating that occurred in association with these specific conditions was equal to or less than +0.6˚C.

MRI-Related Heating, 3-Tesla

In non-clinical testing, the Argus II Implant produced the following temperature rise during MRI performed for 15-min of scanning (i.e., per pulse sequence) in a 3-Tesla (3-Tesla/128-MHz, Excite, HDx, Software 14X.M5, General Electric Healthcare, Milwaukee, WI) MR system: Highest temperature change was +2.1˚C.

Therefore, the MRI-related heating for the Argus II Implant at 3-Tesla using a transmit/receive RF body coil at an MR system reported whole body averaged SAR of 2.9-W/kg indicated that the greatest amount of heating that occurred in association with these specific conditions was equal to or less than +2.1˚C.

Artifact Information

MR image quality may be compromised if the area of interest is in the exact same area or relatively close to the position of the Argus II Implant. Therefore, optimization of MR imaging parameters to compensate for the presence of the implant may be necessary.

Table 6: MRI Artifact Information

Pulse Sequence	Imaging Plane	Maximum Signal Void size - mm²
T1-SE	Parallel	979
T1-SE	Perpendicular	959
GRE	Parallel	2,242
GRE	Perpendicular	3,381

During the MRI Procedure

The MRI technologist should tell the patient to notify the MRI system operator if pain or unusual sensation occurs during the MRI examination. If the patient experiences any pain or unusual sensation, the MRI procedure should be stopped immediately and the source of the problem should be investigated.

Device Functionality

In non-clinical MRI tests, the Argus II implant was exposed to eight different pulse sequences (see Table 7 below) using 1.5-T/64MHz (Symphony, Siemens Medical Solution, Erlangen, Germany) and 3.0-T/128MHz Excite, HDx, Software 14X.M5, General Electric Healthcare, Milwaukee, WI) MR systems. The results indicated that exposing the Argus II implant to these MRI conditions did not damage or alter the function of the device nor did it have adverse effects on the device's functionality. However, it is strongly recommended that the Argus II Implant be tested by a qualified clinician or Second Sight personnel as soon as possible following an MRI procedure to confirm that it is still functioning properly.

Table 7: Summary of MR Imaging Pulse Sequences Used

Sequence #	1	2	3	4	5	6	7	8
Pulse Sequence	T1-SE	T2-SE	T1-FSE	T2-FSE	GRE. 3D	FGRE. 3D	GRE. MTC	EPI
TR (msec)	700	3,000	700	5,000	20	3.7	628	3,400
TE (msec)	10	100	12	113	2.7	1.2	10	103
Flip Angle	N/A	N/A	N/A	N/A	25	8	5	N/A
Field of View (cm)	30	30	30	30	30	30	10	30
Section Thick (mm)	10	10	10	10	3	3	10	1
Imaging Plane	Axial	Axial	Axial	Axial	Volume	Volume	Axial	Axial

T1-SE, T1-weighted spin echo; T2-SE, T2-weighted spin echo; T1-FSE, T1-weighted fast spin echo; T2-FSE, T2-weighted fast spin echo; GRE, gradient echo; 3D, three-dimensional; FGRE, fast gradient echo; MTC, magnetization transfer contrast; EPI, echo planar imaging; N/A, not applicable; GRE, gradient echo; SE, spin echo

ELECTROMAGNETIC ENVIRONMENTS

The essential performance of the Argus II System is defined as the following: During start-up, shut-down, and normal operation of the interfering device, the Argus II System shall not experience:

- A permanent shutdown and/or reset of programmable parameters of the VPU. VPU shutdown during exposure to the interfering device is acceptable but the VPU must retain the ability to power-up after the interfering device is removed. Upon restart of the VPU, all programmable parameters must remain unchanged.

- Any unintended or unsafe stimulation. Unintended stimulation is defined as any stimulation that the VPU is not programmed to instruct the implant to perform. Unsafe stimulation is defined as any stimulation, intended or unintended, that exceeds the balance limit of 5% or the charge limit of 110nC. The charge limit of 110nC is equivalent to the charge density limit of 0.35mC/cm^2 that has been established for the Argus II System.

Guidance and manufacturer's declaration – electromagnetic emissions		
The Argus II system is intended for use in the electromagnetic environment specified below. The customer or the user of the Argus II system should assure that it is used in such an environment.		
Emissions test	**Compliance**	**Electromagnetic environment – guidance**
RF emissions CISPR 11	Group 1	The Argus II system uses RF energy only for its internal function. Therefore, its RF emissions are very low and are not likely to cause any interference in nearby electronic equipment.
RF emissions CISPR 11	Class B	The Argus II System is suitable for use in all establishments, including domestic establishments and those directly connected to the public low-voltage power supply network that supplies buildings used for domestic purposes.
Harmonic emissions IEC 61000-3-2	Not Applicable*	
Voltage fluctuations/ flicker emissions IEC 61000-3-3	Not Applicable*	
* Not Applicable – The Argus II System is Battery Powered		

Guidance and manufacturer's declaration – electromagnetic immunity			
The Argus II system is intended for use in the electromagnetic environment specified below. The customer or the user of the Argus II system should assure that it is used in such an environment.			
IMMUNITY test	**IEC 60601 test level**	**Compliance level**	**Electromagnetic environment – guidance**
Electrostatic discharge (ESD) IEC 61000-4-2	± 6 kV contact ± 8 kV air	± 6 kV contact ± 8 kV air	Floors should be wood, concrete, or ceramic tile. If floors are covered with synthetic material, the relative humidity should be at least 30 %.
Electrical fast transient / burst IEC 61000-4-4	± 2 kV for power supply lines ± 1 kV for input/output lines	Not Applicable	
Surge IEC 61000-4-5	± 1 kV line(s) to line(s) ± 2 kV line(s) to earth	Not Applicable	
Voltage dips, short interruptions and voltage variations on power supply input lines IEC 61000-4-11	<5 % *U*T (>95 % dip in *U*T) for 0,5 cycle 40 % *U*T (60 % dip in *U*T) for 5 cycles 70 % *U*T (30 % dip in *U*T) for 25 cycles <5 % *U*T (>95 % dip in *U*T) for 5 s	Not Applicable	
Power frequency (50/60 Hz) magnetic field IEC 61000-4-8	3 A/m	3 A/m	Power frequency magnetic fields should be at levels characteristic of a typical location in a typical commercial or hospital environment.
NOTE *U*T is the a.c. mains voltage prior to application of the test level.			

Guidance and manufacturer's declaration – electromagnetic immunity			
The Argus II system is intended for use in the electromagnetic environment specified below. The customer or the user of the Argus II system should assure that it is used in such an environment.			
IMMUNITY test	**IEC 60601 Test Level**	**Compliance level**	**Electromagnetic environment – guidance**
Conducted RF IEC 61000-4-6 Radiated RF IEC 61000-4-3	3 Vrms 150 kHz to 80 MHz 3 V/m 80 MHz to 2.5 GHz	3 V 3 V/m	Portable and mobile RF communications equipment should be used no closer to any part of the Argus II system, including cables, than the recommended separation distance calculated from the equation applicable to the frequency of the transmitter. **Recommended separation distance** $d = 1.17\ P$ $d = 1.17\ P$ 80 MHz to 800 MHz $d = 2.33\ P$ 800 MHz to 2.3 GHz where P is the maximum output power rating of the transmitter in watts (W) according to the transmitter manufacturer and d is the recommended separation distance in meters (m). Field strengths from fixed RF transmitters, as determined by an electromagnetic site survey,[a] should be less than the compliance level in each frequency range.[b] Interference may occur in the vicinity of equipment marked with the following symbol: 
NOTE 1 At 80 MHz and 800 MHz, the higher frequency range applies. NOTE 2 These guidelines may not apply in all situations. Electromagnetic propagation is affected by absorption and reflection from structures, object and people.			
[a] Field strengths from fixed transmitters, such as base stations for radio (cellular/cordless) telephones and land mobile radios, amateur radio, AM and FM radio broadcast and TV broadcast cannot be predicted theoretically with accuracy. To assess the electromagnetic environment due to fixed RF transmitters, an electromagnetic site survey should be considered. If the measured field strength in the location in which the Argus II system is used exceeds the applicable RF compliance level above, the Argus II system should be observed to verify normal operation. If abnormal performance is observed, additional measures may be necessary, such as re-orienting or relocating the Argus II System. [b] Over the frequency range 150 kHz to 80 MHz, field strengths should be less than 3 V/m.			

Recommended separation distances between portable and mobile RF communications equipment and the Argus II system

The Argus II system is intended for use in an electromagnetic environment in which radiated RF disturbances are controlled. The customer or the user of the Argus II system can help prevent electromagnetic interference by maintaining a minimum distance between portable and mobile RF communications equipment (transmitters) and the Argus II System as recommended below, according to the maximum output power of the communications equipment.

Rated maximum output power of transmitter (W)	**Separation distance according to frequency of transmitter (**m)		
	150 kHz to 80 MHz d = ⌈ 3.5⌋ PV1	**80 MHz to 800 MHz** d = ⌈ 3.5⌋ PE1	**800 MHz to 2.5 GHz** d = ⌈ 7 ⌋ PE1
0.01	0.0117	0.0117	0.0233
0.1	0.117	0.117	0.233
1	1.17	1.17	2.33
10	11.7	11.7	23.3
100	117	117	233

For transmitters rated at a maximum output power not listed above, the recommended separation distance *d* in meters (m) can be estimated using the equation applicable to the frequency of the transmitter, where *P* is the maximum output power rating of the transmitter in watts (W) according to the transmitter manufacturer.

NOTE 1 At 80 MHz and 800 Hz, the separation distance for the higher frequency range applies.

NOTE 2 These guidelines may not apply in all situations. Electromagnetic propagation is affected by absorption and reflection from structures, objects, and people.

WIRELESS INFORMATION

The Argus II Glasses use wireless technology to communicate with and power the Implant.

Wireless Specifications	
Frequency (to the implant)	3.156 Megahertz (MHz.)
Frequency (from the implant)	473 – 490 Kilohertz (KHz.)
Bandwidth (to the implant)	13 Kilohertz (KHz.)
Bandwidth (from the implant)	20 Kilohertz (KHz.)
Power (to the implant)	Amplitude modulation (AM) Less than 1.2 watts
Power (from the implant)	Frequency shift keying (FSK) Less than 10 microwatts
Wireless Link Performance	Wireless link active more than 90% of the time when the coil is approximately 1 inch (25 mm) or closer to the implant.
Wireless Security	The wireless system is designed so the implant will only operate if it is within a very short distance of the glasses. The Argus II System uses a proprietary communication protocol to reduce the likelihood of inadvertent control or malicious “hacking” of the System. No identifiable personal data are transmitted by the Argus II System.

Wireless Specifications	
Quality of Service	In order for the Argus II System to operate, the external system must be in constant communication with the implant. This communication is achieved through a wireless link between the glasses and the implant. For the wireless link to function, the glasses coil must be in close range (0.78 inches or 20 mm) to the implant. This link does not depend on any other system to function. To better ensure proper functioning of the Argus II System, the glasses should be worn in the same position as they were when they were fitted in the clinic. When the wireless link between the glasses and implant is broken, an alarm will sound and will continue to sound until the wireless link is restored. The link may not function in the presence of large magnetic or radio fields.

STORAGE AND USE

Store the Argus II Implant at temperatures between -10° to 55° Centigrade (14° to 131° Fahrenheit).

Store the Argus II Externals (VPU and glasses) at temperatures between 0° to 45° C (32° to 113° F). Only operate the Argus II Externals at temperatures between 0° to 40° C (32° to 104° F).

HANDLING

The Argus II Implant packaging should be handled with care appropriate to any implantable medical device. Severe impact could damage the storage pack and rupture the sterile packaging.

The Argus II Externals should also be handled with care to avoid dropping, crushing, severe impact, and exposure to water.

SHELF LIFE

A "Use Before" date is located on the Argus II Implant packaging. This date is two years from the date of sterilization.

STERILIZATION

The Argus II Implant and Argus II spare Tacks are supplied sterile with indicators of sterilization. They are sterilized using ethylene oxide. Sterile packs should be carefully inspected to confirm that they have not been compromised. Sterility cannot be guaranteed if the sterile package is damaged or opened. These devices are for single-use only; do not re-sterilize or re-use them.

DIRECTIONS FOR USE & REQUIRED TRAINING

The following are the main steps required to use the Argus II System:

1. Device Implantation
2. Post-Operative Clinical Follow-Up
3. Device Fitting and Training
4. Vision Rehabilitation

In addition to this product insert, several manuals are provided with the Argus II System to provide more detailed instructions for use.

A *Surgeon Manual*, a video describing the surgical procedure and implantation of the Argus II Implant, and hands-on training are provided by Second Sight to all surgeons prior to implantation. The

Surgeon Manual also provides instructions for how to screen potential patients for eligibility for the Argus II System and provides a recommended clinical follow-up schedule. Surgeons must undergo this training in order to implant the Argus II Implant.

A *Device Fitting Manual* is provided to all clinical centers and is included with the Argus II Clinician Fitting System. The Device Fitting Manual provides instruction on how to use all components of the Argus II System. Clinicians and/or technicians must be knowledgeable about state-of-the-art Argus II System fitting procedures. These personnel must be fully trained and qualified by Second Sight in the fitting of the Argus II System.

A *Patient Manual* is provided in print and audio formats to all patients implanted with the Argus II Implant. The Patient Manual describes how to use the external equipment of the Argus II System that is provided to the patient. Argus II System recipients should receive training on all aspects covered in the Patient Manual prior to taking the Argus II External Equipment home for everyday use.
A *Visual Rehabilitation Guide* and hands-on training is provided to low vision therapists who will provide visual rehabilitation to Argus II patients post-implant.

For more information, contact Second Sight using the contact information provided on the front page of this insert.

INTELLECTUAL PROPERTY INFORMATION

Second Sight products (including the Argus II Retinal Prosthesis, Argus II Glasses, Argus II OR Coil, Argus II Video Processing Unit and Argus II Clinician Fitting System) are covered by one or more of the following patents:

United States:

5,109,844, 5,935,155, 5,944,747, 6,165,192, 6,507,758, 6,533,798, 6,718,209, 6,858,220, 6,920,358, 6,949,253, 6,974,533, 7,079,900, 7,097,775, 7,103,416, 7,127,286, 7,133,724, 7,142,909, 7,149,586, 7,181,287, 7,190,051, 7,211,103, 7,224,300, 7,228,181, 7,257,446, 7,263,403, 7,266,413, 7,291,540, 7,314,474, 7,338,522, 7,379,000, 7,480,988, 7,482,957, 7,483,750, 7,483,751, 7,493,169, 7,499,754, 7,527,621, 7,539,544, 7,565,202, 7,565,203, 7,571,004, 7,571,011, 7,574,263, 7,631,424, 7,638,032, 7,645,262, 7,666,523, 7,668,599, 7,676,274, 7,904,164, 7,904,163, 7,904,148, 7894,911, 7,893,909, 7,881,799, 7,877,866, 7,835,798, 7,835,794, 7,818,064, 7,813,796, 7,776,197, 7,818,064, 7,765,009 7,750,076, 7,749,608, 7,738,962, 7,734,352, 7,725,191, 7,709,961, 7,706,893, 7,691,252, 7,887,681, 7,908,010, 7,908,011, 7,912,556, 7,914,842, 7,925,354, 7,926,221, 7,937,153, 7,941,224, 7,957,810, 7,957,811, 7,962,221, 7,989,080,

7,991,478, 8,000,000, 8,010,202, 8,010,206, 8,014,868, 8,014,869, 8,014,878, 8,019,428, 8,034,229, 8,036,751, 8,036,752, 8,046,078, 8,060,211, 8,060,216, 8,068,913, 8,078,284, D565,082, D567565, D599, 313 D600,440

Australia:

2004235629, 2004235627, 2006202503, 2007201542, 2009204164, 776879, 2004205105, 2006202583, 2002252113, 2007201497, 751995, 2003234174, 2003220590, 739523, 2006306658, 2006239178, 2006208146, 2006214142, 2006292220, 2006306660, 2006241404, 2007243163, 2007243164, 2007261384, 2006311850, 2007284422

Europe:

1171188, 1061996, 1061874, 2219728

Japan:

4384363, 3926564, 4411088, 4290566, 3929701

Canada:

2,323,550, 2,323,551

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