NeuroWave
HARNESSING THE POWER OF EEG

Closed Loop Total Intravenous Anesthesia (TIVA) for Combat Casualty Care

- An auto-pilot for safe and effective TIVA delivery -

Presented by Stephane Bibian, PhD
VP Engineering and Clinical Research
NeuroWave Systems Inc.,
2490 Lee Blvd,
Cleveland Heights, OH
sbibian@NeuroWaveSystems.com

STA Meeting
January 2018

NeuroWave
HARNESSING THE POWER OF EEG

ISO 13485
FM 545363

About us…

NeuroWave Systems Inc. was founded in 2003.

- Our mission is to develop, manufacture, and market innovative monitoring and drug delivery devices using advanced signal processing and control system engineering for Anesthesia, Critical Care, and Military Medicine, in order to improve patient safety, outcome and quality of life.
- Our R&D programs are mainly supported through the US Department of Defense and the National Institutes of Health.

Disclosure:
- I am a salaried employee of NeuroWave
- I own stocks in NeuroWave

2

NeuroWave
HARNESSING THE POWER OF EEG

ISO 13485
FM 545363

US Army AutoTIVA Program

3

NeuroWave
HARNESSING THE POWER OF EEG

ISO 13485
FM 545363

Capability Gap

The Army's challenge:

- Anesthesia delivery in Combat Surgical Hospitals has been traditionally handled using a drawover vaporizer that was being discontinued by its manufacturer. At the time, no replacement solution could be readily identified by the DoD.
- Gas anesthesia, while being the standard of care, also suffers from significant drawbacks in terms of logistics. Use of standard of-the-shelf anesthesia gas machines is impractical when considering fielding such units.
- Conversely, Total Intravenous Anesthesia (TIVA) was identified as the "*battlefield anesthetic of the future*" (Barras et al., 2005) "given its safety, simplicity, scientific nature and small logistical footprint".

4

NeuroWave
HARNESSING THE POWER OF EEG

ISO 13485
FM 545363

Capability Gap

TIVA's advantages:

- Lower post-operative nausea and vomiting (reduced workload for post-operative care providers, lower incidence of self injury)
- Does not trigger malignant hyperthermia (difficult/impossible to treat in austere environments)
- Improved hemodynamic stability and temperature conservation
- Fast and predictable recovery and orientation
- Reduced post-operative pain
- Lower ICP
- Simple, low maintenance equipment with small logistical footprint (no need for gas scavenging system, safe for care providers)
- Also associated with lower incidence of post-operative delirium in pediatric patients, and longer survival in cancer surgery patients
- Higher patient satisfaction

Despite the efforts invested by the **Tri-service Anesthesia Research Group initiative on TIVA** (TARGiT) in helping and training service personnel in the administration of TIVA, *its practice is far from wide spread*. It is virtually non existent in CSH and limited at higher echelons of care due to the difficulties in managing the drug delivery, and the lack of familiarity with its administration.

5

NeuroWave
HARNESSING THE POWER OF EEG

ISO 13485
FM 545363

NeuroWave's Solution

- In 2010, we reached out to the Army and proposed to develop a compact intravenous anesthesia delivery *support* system (AutoTIVA), based on standard off-the-shelf infusion pumps.
- The goal of AutoTIVA was to provide Army anesthesiologists with a tool to *enable the safe and effective delivery* of propofol and remifentanil, at all echelons of care, so that combat casualties may have access to the benefits of TIVA.

How?: … by developing a *closed-loop* propofol/remifentanil drug delivery system based solely on *feedback from the brain*.

- **… Auto-pilot/cruise controller** for TIVA
- **Paradigm shift**: from prescribing a dose to prescribing an effect
- **Additional advantages**: reaction time, vigilance, time saving, drug optimization, protocol implementation, closing the expertise gap…

- A contract was awarded to NeuroWave in 2011.

6

We did **NOT** start from scratch!

Early Research Focus

A multi-disciplinary research group (ECEM) was founded in 2001 at UBC and brought together engineers, scientists and clinicians with the goal to improve anesthesia care through *automation, smart monitoring, and data analytics*.

In fact, an early focus was the development of a *closed-loop anesthesia drug delivery system* to control depth of anesthesia (auto-pilot/cruise control).

Two important *technical challenges* were identified and tackled very early on:

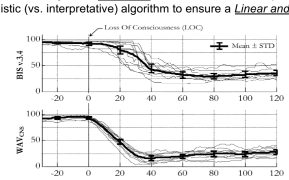
- Lack of a proper sensor technology adapted to closed-loop operation
- Lack of a method to handle patient-variability within a feedback control framework

  …in other words: how can we ensure controller stability in view of patient variability?

Key Technology #1: Sensor

A new algorithm – **WAV_{CNS}** – based on non-invasive EEG-processing was developed in 2000/2002 to resolve some of the limitations of the BIS, in particular:

- Use of Wavelet analysis for *delay-free* characterization of the patient's state
- Deterministic (vs. interpretative) algorithm to ensure a *Linear and Time Invariant* (LTI) behavior



From T. Zikov, "Quantifying cortical activity during general anesthesia…", IEEE TBME, 2006

EEG montage was selected to allow for a bilateral implementation to provide *independent and redundant* WAV_{CNS} values from both sides of the brain simultaneously.

- Good inter-hemispheric reproducibility, where a sustained difference over +/- 8 units is rare in patients with no known neuro-pathologies.

NeuroWave
HARNESSING THE POWER OF EEG

ISO 13485
FM 545363

Key Technology #1: Sensor

- **Rapid response** (no calculation delay)
- **LTI behavior** (no switching algorithms)
- **Index robustness** (high level of inter-hemispheric agreement)

… makes the WAV_{CNS} well suited for use as feedback sensor…

…and also well suited as a simple monitoring tool!

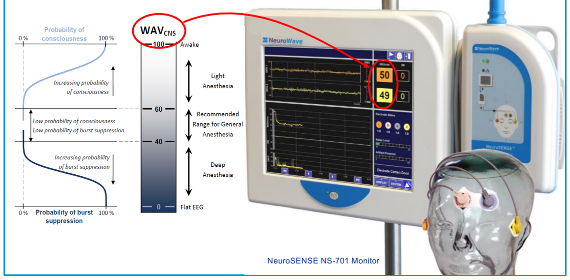
10

NeuroWave
HARNESSING THE POWER OF EEG

ISO 13485
FM 545363

Key Technology #1: Sensor

Members of the UBC research group patented the sensor technology in 2002 and licensed it to Cleveland Medical Devices (NeuroWave division).



NeuroSENSE NS-701 Monitor

11

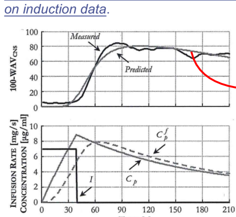
NeuroWave
HARNESSING THE POWER OF EEG

ISO 13485
FM 545363

Key Technology #2: Controller

Inter-patient variability can be readily observed by deriving PK/PD models for a given population of patients.

Leveraging the delay-free/LTI characteristics of the WAV_{CNS} sensor, we have shown that *PD parameters can be identified based simply on induction data*.



Patient #	ASA	Age [yrs]	Weight [kg]	Height [cm]	Gender	T_d [s]	k_d [$s^{-1} \cdot 10^{-3}$]	EC_{50} [$\mu g/ml$]	E_0	γ
G1: ≥18 - <30 yrs										
007	nc	21	100	178	M	22	133.5	3.2	98.3	4.7
008	nc	28	59	168	F	4	44.4	3.1	99.7	2.5
010	2	26	90	190	M	44	25.0	2.4	96.1	2.0
015	2	21	53	157	F	45	51.5	3.8	100.0	1.2
016	2	19	90	185	M	39	85.7	3.8	98.4	2.3
023	1	28	60	162	F	18	82.5	3.9	100.0	2.1
030	1	24	78	170	M	32	44.4	2.9	97.5	2.7
035	2	19	68	164	F	12	26.7	1.9	93.8	2.1
038	2	25	70	170	M	7	35.2	3.4	98.0	1.9
046	1	23	81	180	M	9	32.8	2.8	97.5	2.8
048	1	18	83	178	M	17	46.4	2.8	99.8	2.3
053	2	21	67	163	F	4	26.2	2.4	100.0	2.5
058	1	22	88	183	M	9	50.4	2.5	96.1	2.6
066	1	21	59	162	M	18	160.5	3.6	100.0	4.1
071	1	19	72	176	M	20	75.0	2.5	99.6	1.9
Mean		**22.3**	**74.5**	**172**		**20.0**	**61.4**	**3.0**	**98.3**	**2.5**
G2: ≥30 - <40 yrs										
006	nc	34	73	[illegible]	M	44	54.8	3.2	99.6	2.6
009	nc	34	71	178	M	29	83.1	4.0	94.5	2.3
029	1	35	[illegible]	189	M	18	34.4	3.7	99.5	2.1
036	1	38	85	180	M	1	29.6	3.3	80.2	1.9
047	1	33	86	168	F	1	24.9	3.1	98.3	1.5
049	2	38	75	176	M	12	35.2	3.9	98.9	1.8
051	1	39	91	178	M	4	24.8	2.7	91.4	2.0
061	1	34	78	178	M	12	28.7	2.8	99.0	2.3
063	1	36	65	163	F	5	27.0	2.8	96.2	2.1
065	1	34	58	157	F	4	67.2	3.6	98.5	2.0
068	2	33	77	180	M	12	29.3	3.1	98.7	1.8
074	2	39	105	185	M	13	29.1	3.7	93.4	1.9
Mean		**35.6**	**79.6**	**176**		**12.9**	**39.0**	**3.3**	**95.7**	**2.0**
G3: ≥40 - <50 yrs										
004	nc	49	80	177	M	35	38.0	3.3	99.0	1.8
025	1	46	66	168	F	11	36.6	6.1	99.4	1.3
027	2	45	99	182	M	2	32.6	4.7	98.1	1.3
040	1	48	77	173	M	12	35.0	4.5	97.0	1.4
042	1	47	98	189	M	10	28.7	3.9	96.3	2.1
043	1	46	79	172	M	12	34.8	3.9	96.9	1.8
052	1	40	96	193	M	9	36.6	3.2	95.4	2.0
069	2	40	77	176	M	8	35.6	3.4	94.3	2.5
072	1	48	97	190	M	13	30.0	3.0	95.0	2.0
Mean		**45.4**	**85.4**	**180**		**12.4**	**34.2**	**4.0**	**96.8**	**1.8**
G4: ≥50 - ≤60 yrs										
018	2	60	63	165	F	3	31.5	3.5	95.8	2.4
033	3	52	91	185	M	29	42.0	4.4	88.8	2.5
041	2	52	100	182	M	2	21.8	4.7	89.5	1.7
057	1	52	97	176	M	16	28.8	3.7	89.4	1.4
060	1	50	95	183	M	10	26.4	4.0	97.5	2.0
064	2	52	56	173	F	6	58.0	5.0	91.5	1.9
070	2	54	100	180	M	6	32.2	4.2	99.0	1.5
075	3	60	95	176	M	12	24.3	3.1	98.6	1.8
Mean		**54.0**	**87.1**	**177**		**10.5**	**33.1**	**4.1**	**93.8**	**1.9**

S. Bibian et al., "Patient variability and uncertainty quantification in anesthesia", IFAC, 2006

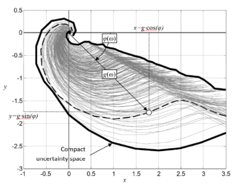
12

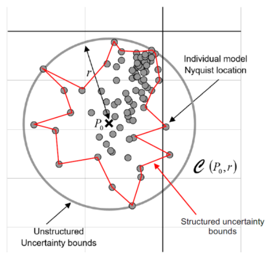
NeuroWave
HARNESSING THE POWER OF EEG

Key Technology #2: Controller

ISO 13485
FM 545363

We have further shown that patient variability over the study population can be *mathematically described* using the relative multiplicative uncertainty framework:





$P = P_0 + r \cdot \Delta$, where $\Delta \in \mathbb{C}, |\Delta| \leq 1$

$P = P_0 \cdot (1 + W_P \cdot \Delta)$, where $W_P = \frac{r}{P_0}$

uncertainty weight

S. Bibian et al., "Closed-loop target controlled infusion systems: Stability…", J. Mil. Med., 2015

NeuroWave
HARNESSING THE POWER OF EEG

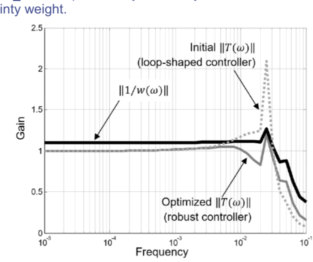
Key Technology #2: Controller

ISO 13485
FM 545363

A linear, fixed controller can be shown to be mathematically stable for any patient model inscribed within the uncertainty bounds *if* the complementary sensitivity function does not exceed the inverse of the uncertainty weight.

Robust Stability (RS) condition

- The controller parameters can be further optimized such that to provide the highest gain (i.e., fast reaction) *without violating the RS condition*.
- Mathematical proof of stability in view of patient-variability.



S. Bibian et al., "Closed-loop target controlled infusion systems: Stability…", J. Mil. Med., 2015

NeuroWave
HARNESSING THE POWER OF EEG

Key Technology #2: Controller

ISO 13485
FM 545363

Dual propofol/remifentanil controller:

- The sole control of hypnosis using propofol will not provide anesthesiologists with the full benefits of automatization. In fact, *dual control* of hypnosis and analgesia is highly desirable.
- In 2006, we hypothesized that a controller designed for the control of the WAV_{CNS}, and based on the co-administration of propofol and remifentanil, may provide faster tracking and disturbance rejection.
  - The brain is NOT the end-target organ of opioids. However, we have frequently observed that lack of proper analgesia results in sudden cortical arousal in the presence of nociception.
  - We hypothesized that a dual propofol/remifentanil controller could be designed, where the controller first uses remifentanil to compensate for the high frequency transients, while propofol is only used to compensate low frequency transients. This method would work due to the faster PK/PD of remifentanil.
- This dual control concept was successfully clinically tested in France (MedSteer/Foch), Canada (iControl/UBC) and India (CLADS) over the past 10 years.

NeuroWave
HARNESSING THE POWER OF EEG

ISO 13485
FM 545363

Early Prototype

A first prototype of the AutoTIVA, integrating both our WAV_{CNS} sensor and the dual controller, was built in 2012

Limitations:

- We realized that infusion pumps approved for human use cannot be remotely controlled without voiding regulatory approval.
- We reached out to pump manufacturers to discuss the possibility of interfacing their pumps (or creating a specific remotely controllable pump version for the purpose of this application). Regulatory hurdles and costs were major issues.
- Another problem was the multiplicity of user interfaces, which adversely affects human factors and requires additional training.
- Hardware complexity/cabling was another weakness of the proposed solution…

16

NeuroWave
HARNESSING THE POWER OF EEG

ISO 13485
FM 545363

US Navy's ACCS AutoSED Module

17

NeuroWave
HARNESSING THE POWER OF EEG

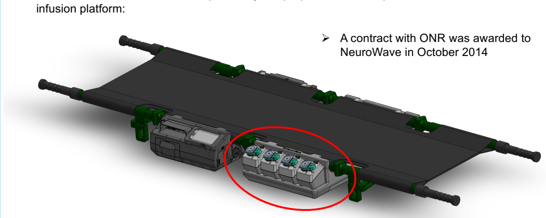
ISO 13485
FM 545363

The Navy ACCS

In 2014, the Office of Naval Research reached out to NeuroWave to add sedation and fluid delivery to their Automated Critical Care System (ACCS) platform, a fully _instrumented_ NATO litter designed for _prolonged field care_, _remote operation_, and long distance _unmanned en-route care_.

- In order to meet the Navy's objectives, we proposed to first develop an infusion technology suitable for en-route care. More specifically, we proposed to develop a robust modular 4-channel infusion platform:

- A contract with ONR was awarded to NeuroWave in October 2014

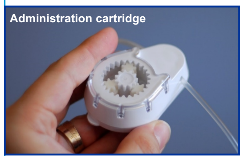


18

NeuroWave
HARNESSING THE POWER OF EEG

Key Technology #3: Infusion Pump

ISO 13485
FM 545363


Administration cartridge

- Dual epicyclic gear to minimize friction and tube pull
- Inherent free-flow prevention
- Geometric pumping chamber design to minimize flow pulsation at low speeds
- Twist-and-lock features for rapid and error-free insertion
- Pressure sensors for upstream and downstream occlusion detection
- Transparent cover to facilitate visual inspection
- 2 variants: low flow (up to 1,200 mL/hr) and high flow (up to 4,000 mL/hr)
- Flow accuracy +/-5%

- Bayonet-style mechanism for quick and easy cartridge insertion
- Compact enclosure houses a light stepper motor
- Lighted edge for improved usability
- Water ingress and ESD protection

Pump Head Module

NeuroWave
HARNESSING THE POWER OF EEG

ISO 13485
FM 545363

Bringing it all together

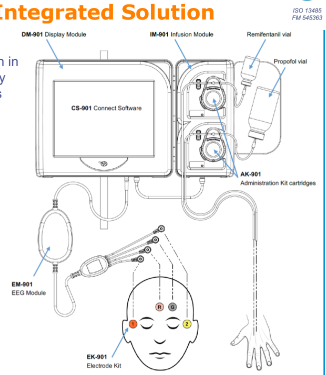
NeuroWave
HARNESSING THE POWER OF EEG

Vertically Integrated Solution

ISO 13485
FM 545363

We reached out to the US Army again in 2015 and proposed to add the Navy infusion technology to the previous AutoTIVA platform.

- Development work was started in late 2016



NeuroWave
HARNESSING THE POWER OF EEG

ISO 13485
FM 545363

Current Platform

22

NeuroWave
HARNESSING THE POWER OF EEG

ISO 13485
FM 545363

Regulatory Considerations

23

NeuroWave
HARNESSING THE POWER OF EEG

ISO 13485
FM 545363

Regulatory Considerations

SPECIAL ARTICLE

Regulatory Considerations for Physiological Closed-Loop Controlled Medical Devices Used for Automated Critical Care: Food and Drug Administration Workshop Discussion Topics

Bahram Parvinian, MS,*† Christopher Scully,
and Sandy Weininger, PhD†

Part of the mission of the Center for De
and Drug Administration is to facilitate
important role in helping its stakeholde
patients, patient advocates, academia,
landscape for medical devices. This is particularly important for innovative physiological closed-loop controlled (PCLC) devices used in critical care environments, such as intensive care units, emergency settings, and battlefield environments. CDRH's current working definition of a PCLC medical device is a medical device that incorporates physiological sensor(s) for automatic manipulation of a physiological variable through actuation of therapy that is conventionally made by a clinician. These emerging devices enable automatic therapy delivery and may have the potential to revolutionize the standard of care by ensuring adequate and timely therapy delivery with improved performance in high workload and high-stress environments. For emergency response and military applications, automatic PCLC devices may play an important role in reducing cognitive overload, minimizing human error, and enhancing medical care during surge scenarios (ie, events that exceed the capability of the normal medical infrastructure). CDRH held an open public workshop on October 13 and 14, 2015 with the aim of fostering an open discussion on design, implementation, and evaluation considerations associated with PCLC devices used in critical care environments. CDRH is currently developing regulatory recommendations and guidelines that will facilitate innovation for PCLC devices. This article highlights the contents of the white paper that was central to the workshop and focuses on the ensuing discussions regarding the engineering, clinical, and human factors considerations. (Anesth Analg 2017;XXX:00–00)

"… may have the potential to revolutionize the standard of care by ensuring adequate and timely therapy delivery with improved performance in high workload and high-stress environments."

From B. Parvinian et al., "Regulatory Considerations …", A&A, 2017

24

Regulatory Considerations

Table 3. Concept of Level of Automation Applied to an Example of a Physiological Closed-Loop Controlled Medical Device

Medical Device LOA	Task	Example Neonatal Oxygen Therapy
1	Manual therapy. All decisions pertaining to care of the patient as related to a specific therapy are made by the clinician. The device does not provide decisions nor does it provide recommendations	Clinician determines oxygen therapy is needed. Makes FiO_2 adjustment for a hypoxemic patient based on vital signs, SpO_2 monitor, and overall status of the patient. Clinician decides when to wean
2	Partial automation. Clinician determines the type of therapy that is needed, determines the input target/range. The device actuates automatically to keep the patient on target or within the prescribed range. All set points are determined by clinician	Clinician determines the patient needs oxygen therapy, inputs the prescribed range of SpO_2 between 90% and 95%. Device senses SpO_2 of 80% and increases FiO_2 by 50% automatically to keep the patient SpO_2 between 90% and 95% as determined by clinician. Clinician decides when to wean
3	High automation. The clinician determines the type of therapy that is needed and prescribes the first target range or set point. Device actuates to keep the patient within target prescribed range but determines and adjusts the subsequent set points automatically. Clinician will have override capabilities to assume manual care at any time	Clinician determines the patient needs oxygen therapy. Device senses SpO_2 of 80% and increases FiO_2 by 50% autonomously to keep the patient SpO_2 between 90% and 95% as determined by the device algorithm. The clinician decides when and how to wean
4	Full automation. Device determines type of therapy. Determines the set points and course of oxygen delivery as well as initiation and rate of weaning. Clinician will have override capabilities to assume manual care at any time	Device determines oxygen therapy is needed and autonomously delivers oxygen to keep SpO_2 within a range of 90%–95% as determined by device. The device determines when and how the patient is going to be weaned from oxygen. Clinician can always intervene

Abbreviations: FiO_2, fraction of inspired oxygen; LOA, levels of automation; SpO_2, peripheral capillary oxygen saturation.

From B. Parvinian et al., "Regulatory Considerations …", A&A, 2017

Regulatory Considerations

- Sensor (validity, *latency/dynamics*, robustness and reliability)
- Controller design (*inter-patient variability* considerations, *conformity to the drug label*, handling of non-linearities, etc…)
- Preclinical evaluation (*analytical evaluation*, evidence of safety, and *performance evaluation* under faults conditions)
- Implementation (safety features and *fallback modes*, archive)
- Clinical use & usability (adequacy of WAV_{CNS}, operational transparency, simulator-based training, etc.)

Table 2. Regulatory Considerations for Design, Development, and Preclinical Evaluation of PCLC Medical Devices Used in Critical Care Environments

Sensor considerations
- Sensor validity and how accurately the sensed quantity represents the controlled variable. For example, if end-tidal anesthetic agent is being measured as feedback and surrogate quantity to adjust anesthetic gas concentration in the blood ultimately brain, consider providing a clinically robust justification for validity of this surrogate
- Characterizing sensor latency and potential detrimental effects on controller stability and inadequate therapy delivery
- Sensor robustness which may be thought of as the sensor's continuous valid performance in face of patient variabilities/uncertainties
- Sensor reliability and resilience which may be defined as valid performance of the sensor in face of environmental uncertainties. For example in case of automated anesthesia delivery based on EEG-derived sensors, consider the effect of concomitant drugs (eg, neuromuscular blockers), motion artifact, and surgical disturbance (eg, electrocautery artifact) on the sensed depth of hypnosis

Controller design considerations
- Quantifying various types of uncertainties including but not limited to dynamic uncertainty imposed by inter and intra patient variability for the purpose of controller design
- Establishing a criteria for model selection and model optimality in design based on clinical context of use
- Pitfalls (eg, lack of established methods to determine stability and robustness) that may hamper system analysis and evaluation
- Potential additional validation activities that may ensue as a result of model-free design approach (eg, extensive simulation studies)
- Verifiable and structured methodologies for control system tuning during the design stage
- Designing the system with particular attention to nonlinearities in the whole system (eg, actuator saturation, plant, and sensor nonlinear behavior) which may result in system instability and failure
- Control algorithm conformity to the drug label

Clinical use considerations
- Relation between clinical outcomes and sensed/controlled variable(s) and the criteria that make a control variable appropriate for PCLC applications should be considered
- User interface design to provide operational transparency to the clinical users especially for device output is an important consideration
- Physical controls and display elements to improve user perception, cognition, and responses
- Information that needs to be conveyed to the user when reverting to an open-loop or completely manual control such that the state of the patient and previous delivered therapy is clear for the operator
- Specific environments of use (ie, hospital versus en route transport) may affect the interface design and how the PCLC medical device is used
- Design features to allow a clinician to recognize if a patient may not be responsive, or response changes, to therapy controlled by PCLC medical device
- The limitation of PCLC medical device in terms of delivering therapy based on a single sensor as compared with manual care where multiple factors are considered by the user
- System complexity and the training needed to ensure safe device use
- Including instruction for use language to enhance operational transparency and to create a mental model for the user of the PCLC medical device

Usability/human factors considerations
- Clinical setting, use scenarios, and potential for infrequent but critical events should be considered
- Simulator based training approaches may be leveraged to evaluate safety and assess human–automation interactions
- Depending on the level of automation, analysis techniques for identifying hazards such as overreliance and complacency may need to be considered
- Evaluating the effectiveness of any risk mitigation strategies for automation-induced hazards such as overreliance and/or complacency
- Language in the instruction for use should increase understanding and transparency of the controller operation

Implementation considerations
- Interoperability of system components such as pumps and sensors should be considered
- Implementing safety features and fallback modes for system fail-safe operation
- The need for data capture to allow forensic data and failure root cause analysis

Preclinical evaluation considerations
- Aiming to assess the performance of the whole system (controller, device components, patient, use environment)
- Analytical, bench computational (eg, in silico and hardware-in-the-loop), and animal testing or combination of these testing methods
- Analytical approaches for nonclinical assessment may depend on controller design (eg, knowledge-based; proportional, integral, and derivative; model-predictive control)
- Providing evidence of safe system performance (eg, stability) during inter and intra patient variability and disturbances that can be expected clinically
- Verifying functionality of fault detection and fallback modes
- Verification, validation, and uncertainty quantification of computational physiological models used for in silico and hardware-in-the-loop evaluation studies
- Animal testing needs to consider physiological and anatomical differences between animal model and human. Consider establishing clinical relevance of the animal model

From B. Parvinian et al., "Regulatory Considerations …", A&A, 2017

Take home message

NeuroWave
HARNESSING THE POWER OF EEG

ISO 13485
FM 545363

Closed-loop TIVA is both **technically and clinically feasible**

- The AutoTIVA concept (EEG-based dual controller for propofol and remifentanil) has been *clinically validated in thousands of cases* by research teams from Canada, France, and India.
- Leverages the *benefits of TIVA and brain monitoring*. The closed-loop function acts as a force multiplier.

The AutoTIVA is a **vertically integrated solution** combining 3 key technologies: brain monitoring, infusion pump, and robust controller, developed by UBC/NeuroWave

- Fully functional pilot product optimized for manufacturability
- Regulatory approval (FDA) will be sought, as the AutoTIVA transitions to an Advanced Development program at USAMMA.

The FDA has indicated **strong interest** in PCLC technologies, **and is being supportive of sponsors** willing and capable to bring applications for review.

- Their feedback *has guided our design* since early on.

Funding from the **US Army** (Medical Research and Material Command) and the **Office of Naval Research** is gratefully acknowledged.

- Their *continuing support* has been extremely important to get this project moving forward.
- More than just a funding Agency, they are partners with whom we often interact to refine operational concepts, and system specifications. They will likely be our first end-users.

28