HOW SAFETY FEATURES MAKE OR BREAK INFUSION PUMP DESIGN

In this article, Charlotte Harvey, Medical Sector Manager, and Tim Frearson, Senior Consultant, both of Sagentia, overview the safety systems required when designing an infusion pump system, with a focus on free-flow prevention, occlusion detection and air-in-line detection.

Infusion pumps are complex electromechanical devices used to deliver fluids into a patient's body in a controlled manner. They typically serve the needs of hospital-bound patients, where life-saving medication is normally delivered via intravenous infusion. With the desire for patients to be able to manage their own conditions outside of a hospital setting, together with the trend towards continuous drug delivery, the use of at-home, ambulatory and wearable infusion pumps is on the rise.

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New entrants to the world of infusion pumps will find that safety features are a major driving force behind their design, as they control every aspect of a user's interaction with the device and have the potential to make it unusable when things go wrong. This article reviews different pump types, their typical safety features, and the implementation of three of the most important safety features in infusion pump design.

IDENTIFYING THE DIFFERENT TYPES OF INFUSION PUMP

There are several types of infusion device. The type of pump used is dependent on the patient's needs, such as the required volume and the speed of the desired infusion. And different types of pump are more or less suited to hospital, at-home or ambulatory usage.

In hospital settings, volumetric, syringe and gravity pumps are the most popular choices. Volumetric pumps (Figure 1), sometimes referred to as large volume pumps (LVPs), are the preferred choice

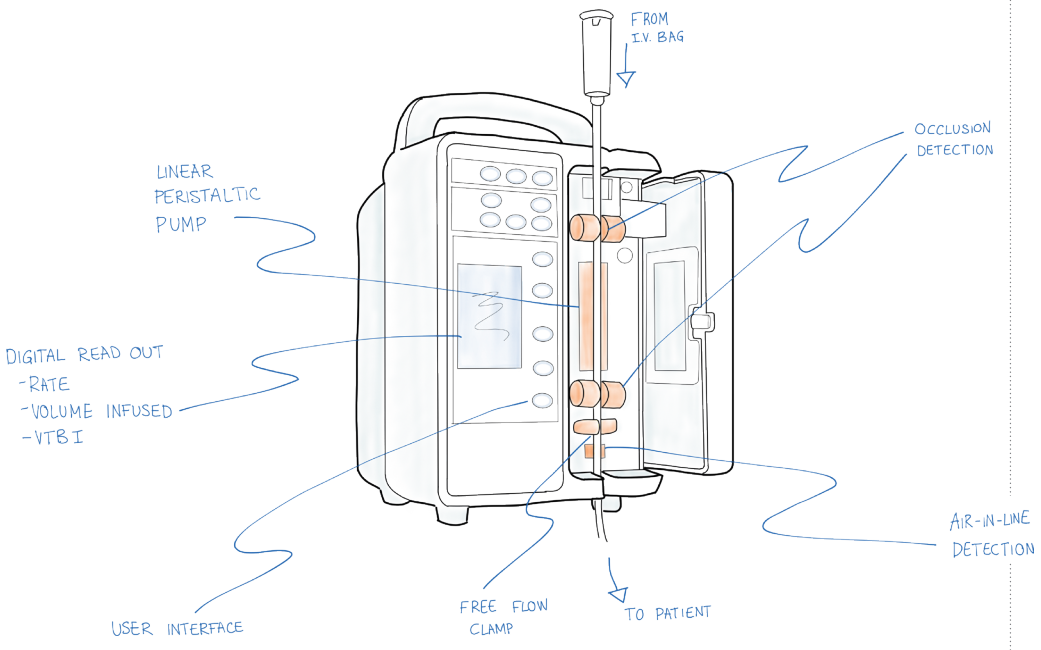

Figure 1: A typical volumetric infusion pump.

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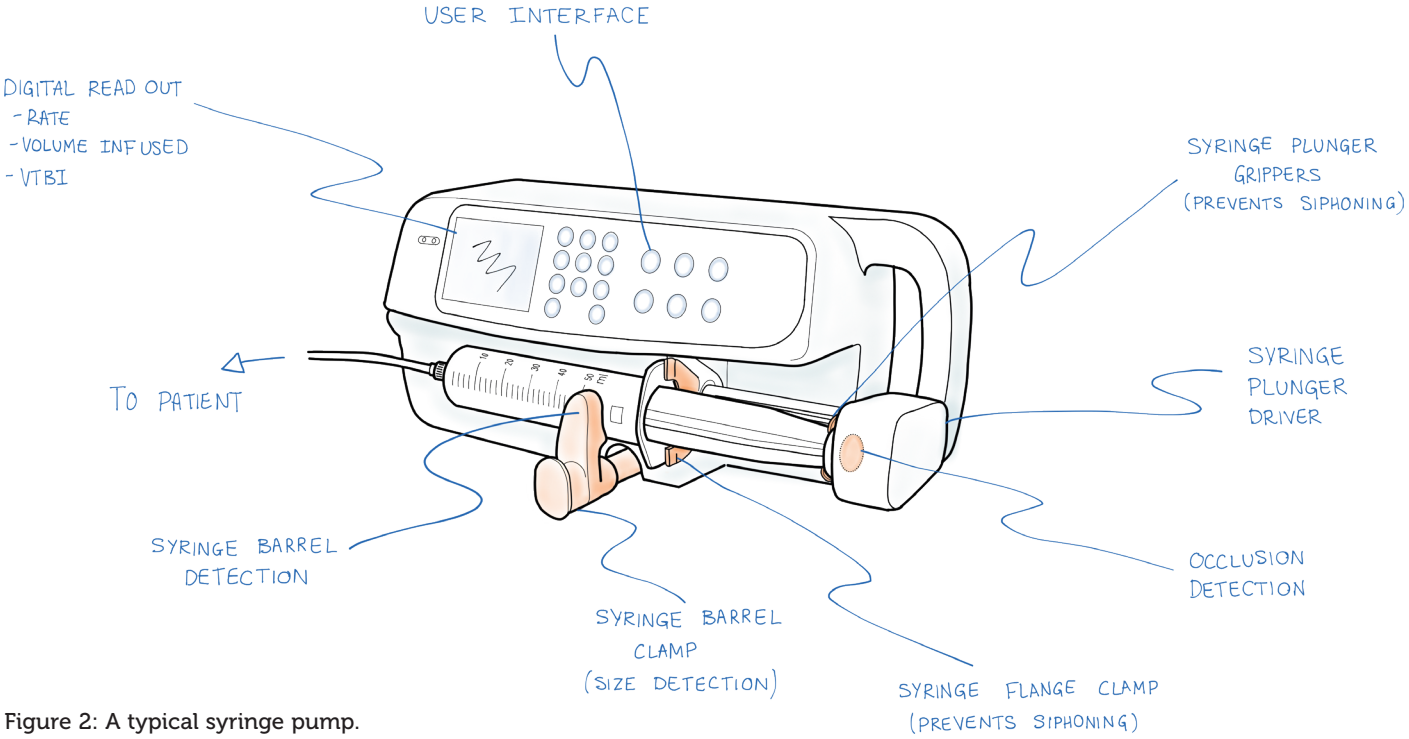

Figure 2: A typical syringe pump.

for medium and high flow rates and large volume intravenous or enteral infusions. They use a pumping action (typically linear or rotary peristaltic) to pump fluid into the patient under pressure and resistance. An IV bag can be used, or the device may employ a dedicated cassette.

For lower volume delivery and lower infusion rates, syringe pumps (Figure 2) are usually the preferred option. They work by pushing the plunger of a disposable syringe along at a predetermined rate. This rate can be continuous or in steps, delivering several boluses in a given time. Pumps for delivering anaesthesia for sedation are based on the syringe mechanism. They are specially designed so that the rate can be adjusted, and other functions accessed, during infusion. These pumps allow for a higher flow rate, so that the induction dose can be delivered quickly in a single operation.

Some infusions are given using gravity rather than a device to deliver the fluid. Gravity pumps rely on the head height of the fluid bag relative to the point of delivery to the patient. A gravity-controlled infusion employs a clamping action to vary the flow of liquid. The speed of delivery is dependent on pressure differential, which can be limited, but the volume is almost limitless. A gravity infusion would be employed when the rate of infusion can be imprecise and large volumes are required.

Pump types that are more suited to at-home or mobile use are elastomeric, patient-controlled analgesia (PCA) and "wearable" pumps. Elastomeric pumps are non-electronic single use pumps, with an elastomeric balloon reservoir that empties itself with a fixed pressure. They are generally designed for use by a patient at home as they are small, lightweight, easy to use and are easily portable. They are primarily intended to deliver antibiotics, chemotherapy and analgesics where a high degree of accuracy is not required. The downside to these types of pump is they have no built-in alarms or event log. Both temperature and the fill volume of the reservoir (under- or over-filling) can affect the intended delivery rate. Conversely, the fixed volume and flow-rate reduce the risk of user error.

Patient-Controlled Analgesia (PCA) pumps allow a patient to control the delivery of pain-relieving medication. Typically, the syringe pump design allows patients to deliver a bolus themselves. Protection against free-flow is especially important with PCA pumps due to the nature of the medication involved (pain relief) and risk of overdose, particularly if the patient may be unsupervised for some of the time.

There are also pumps specifically designed to allow patients to continue receiving treatment or therapy away from a hospital, thereby leading a normal life during treatment. These are usually referred to as ambulatory pumps and have a size and design that makes them wearable. Wearable solutions vary from ones that adhere to the skin, to ones supplied in a backpack or shoulder-bag. These pumps usually use the volumetric or syringe pump models as a basis for the technology, but are often designed to be more specific to a single drug. Size and usability become larger concerns and significantly impact the device design.

Other types of infusion devices not included here are pneumatic, clockwork and spring. However, these are significantly less common than volumetric and syringe pumps, which will be the focus of discussion in the rest of the article. Many of the learnings from these types of pumps are also relevant to ambulatory or wearable pumps, as they are typically based on the larger volumetric or syringe devices.

DESIGNING FOR SAFETY

The reliability of medical devices such as infusion pumps is extremely important because they are used on patients likely to be in a critical condition. For this reason, they typically incorporate warnings and alarms.

Many of the safety features common to infusion devices are particularly susceptible to tolerance variation of components and assembly processes. Therefore, a large part of designing these features must be dedicated to fully understanding their intended use, clinical environment and potential variations in manufacturing. Getting the design right upfront is critical to ensuring that the design is robust in the field. Some design issues may not present themselves until the product is released into manufacturing where the extreme of tolerance variation is encountered. Due to the adverse events that can occur in the field, there is heavy regulatory focus on their design.

Box 1 shows a list of typical safety features in descending order of importance. Note that a number of these safety features are usability based, to protect against misuse. Note also that the importance of these features does not always correlate with the ease of implementation during device design and development. In the rest of this article the focus will be on free-flow protection, occlusion detection and air-in-line.

ASSESSING FREE-FLOW PROTECTION FEATURES

Over-infusion is known to be a major cause of fatal adverse events when considering infusion pumps. There are a few key differences between free-flow in a syringe pump and in a volumetric pump. In volumetric pumps, free-flow may occur if the disposable tubing is not correctly fitted, or if the fluid is under the action of gravity without the tubing being correctly pinched or clamped. In either of these cases, there are device alarms which can be used to alert the user or caregiver. If free-flow becomes an issue in a syringe pump, the syringe plunger or barrel must not have been correctly loaded, with the pump at a height sufficient to generate a pressure that overcomes the venous pressure and the friction between the plunger and barrel. Warnings and alarms will typically be used to alert the user or caregiver to incorrect syringe loading. Other precautions may include positioning the pump level with the patient and use of an anti-siphon valve.

UNDERSTANDING OCCLUSION DETECTION

Perhaps a more complex system to consider when assessing its robustness in the field (when subject to manufacturing variation) is the occlusion detection subsystem. An occlusion is a common occurrence during an infusion, which occurs when there is an obstruction or closure of the fluid pathway or vessel. Clearly, an occlusion is an issue as it means a patient is not receiving their medication (or other fluid). In some critical applications involving the use of drugs which have a short half-life and result in an immediate pharmacological or physiological response (e.g. adrenaline, dopamine, dobutamine, dopexamine, insulin) the plasma concentrations of drug may drop rapidly following cessation of delivery. In the case of short half-life vasoactive drugs used to maintain cardiac output, it is known that the patient's condition can deteriorate rapidly if the infusion stops. However, occlusions also introduce the risk of a post occlusion bolus, where the pressure in the line builds behind the occlusion and releases suddenly when it clears. As previously mentioned, over-infusion is a major cause of fatal adverse events involving infusion pumps.

Infusion devices typically require high pressures, due to high resistance in the delivery system. This resistance to flow comes from both the body itself and elements in the fluid path, such as filters, anti-siphon valves, compliance in the tubing, the cannula and any potential kinking of the tubing. Additionally, more viscous medications increase the required delivery pressure. The active pumping mechanisms used in syringe and volumetric pumps generate high pressures to overcome this resistance, and therefore the pressure in the line will increase further when an occlusion occurs. Thus, occlusion detection devices typically use force measurement to detect this increase in pressure.

There are key differences in how this is implemented in volumetric and syringe pumps. In volumetric pumps, it is common practice to determine the occlusion status by coupling a force sensor directly to the wall of the disposable pumping segment. As the internal fluid pressure increases or decreases the tubing will exert more or less force on the sensor (Figure 3). To ensure adequate coupling, the disposable tube must be compressed to provide a pre-load force baseline for the sensor. This system can be used to detect a flow restriction either between the pumping mechanism and the administration site (downstream occlusion) or between the medication bag and the pumping mechanism (upstream occlusion). Depending on the pumping mechanism design, a single sensor can detect both.

This type of implementation can be very susceptible to manufacturing variance. However, proper calibration can remove variation in the assembly, signal processing, force sensor, mechanical parts, etc, and software algorithms can be utilised to manage drift and hysteresis. The greatest concern is variation in the disposable tubing (such as wall thickness), as this can lead to large differences in the force sensor output voltage. Batch-to-batch variation means it can be difficult to calibrate out this variance.

Many devices have predetermined occlusion pressure thresholds at which the

BOX 1: TYPICAL SAFETY FEATURES FOR INFUSION DEVICES

- Anti-free-flow device in administration set
- Free-flow clamp in pump when door opened (volumetric pump only)
- Air-in-line detection (volumetric pump only)
- Detection of an empty drug/fluid reservoir
- Occlusion detection
- Provision against accidental modification of settings
- Two distinct actions to change rate
- Two distinct and/or simultaneous actions to initiate bolus
- Syringe barrel clamp alarm, door open alarm or equivalent
- Syringe plunger disengagement alarm or equivalent
- Automatic switching to keep the vein open (KVO) rate at the end of infusion
- Pre-set control of the total volume to be infused and digital read-out of volume infused
- Patient history log and technical history back-up
- Battery back-up (automatic switching to battery when mains power fails)

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device will trigger an alarm, with this being adjustable by the user or caregiver. The positioning of this threshold is important. Set too high, the chance of harmful effects on the patient prior to the alarm sounding are increased (longer time to alarm resulting in a delay to medication delivery). Set too low, the number of nuisance alarms may go up, leading to customer complaints. Infusion pumps undergo vigorous testing of safety critical features (such as occlusion pressure, and time to alarm on occlusion) to ensure patient safety during administration.

On the other hand, measurement of pressure inside a syringe pump is typically performed by measuring the force needed to compress the syringe plunger. This will detect an occlusion in the infusion line or tubing between the syringe and administration site.

Force can be measured here in one of two ways. One implementation is to place a force sensor into the transmission of the drive mechanism to determine resistance as the mechanism pushes the plunger. However, this can be susceptible to manufacturing variation and design tolerance. A more common implementation involves placing a force sensor on the end of the syringe plunger, providing a much more direct measurement of the force required to compress the syringe plunger.

Regardless of implementation, the result is a force-pressure calculation which then requires set occlusion pressure alarm thresholds in the device. However, even with calibration there can be large variance due to the variation in the syringe itself, which is typically not controlled by the pump designer/manufacturer.

Above all, the greatest concern with syringe pumps is the variation in plunger friction. It typically does not influence volumetric accuracy, except at low flow-rates where slip-stick may cause poor flow uniformity, but it does affect pressure-reading accuracy. Higher friction means a higher operating pressure, and thus a shorter time to occlusion alarm for any given pressure alarm threshold. Conversely, lower friction provides a lower operating pressure reading and would result in a longer time to alarm following an occlusion. This problem is eliminated by users, as it is clinical best practice to use the occlusion system as a relative system and set the alarm threshold within a few selectable levels of the average operating infusion pressure. However significant friction variation is not always well accounted for, and users may perceive poor device performance.

EXAMINING AIR-IN-LINE SUBSYSTEMS

Small volumes of air injected intravenously are considered a hazard. Syringe pumps typically do not employ air-in-line detection systems, as they deliver medication from a prepared syringe, with it falling to the caregiver to ensure that air is removed from a syringe before use, or a prefilled syringe. Volumetric pumps, on the other hand, provide mechanisms for preventing the pumping of air into the patient's venous system or incorporate an air-in-line detection system where, if excessive air is detected in the line, the device stops the infusion and generates an alarm to alert the caregiver. Real air-in-line alarms are a result of unacceptable volumes of air detected in the infusion line.

Developing an air-in-line detection system within volumetric pumps is challenging as the robustness of the system is affected by many factors, including flow rate, manufacturing variance, clinical environment (head height of device relative to patient), medication properties (viscosity), detection technology employed, software and calibration, to name just a few! Typically, an air-in-line detection system utilises a pair of ceramic ultrasonic sensors in tandem with software algorithms to detect the presence of air in the infusion line. An alarm would occur when the sensor detects either a series of smaller air bubbles (that equate to a dangerous total sum of air) or a continuous/single air bubble that is of an unacceptable volume.

Nuisance air-in-line alarms are due to misdetection and may occur due to the device being too sensitive, which can lead to customer complaints. Nuisance alarms can also occur for other reasons:

- Tube decoupled from sensor (requires careful design of the interface between the disposable part and the device where the sensors are located)
- Bubbles bouncing within the infusion line (requires careful consideration on the type of mechanism and geometry around the sensors to prevent bubbles forming on the internal wall of the disposable tube, as well as the software algorithms employed in the detection of air).

Conversely, a device that is insensitive may not detect unacceptable volumes of air, which may lead to patient harm. It is important that these devices have a high level of accuracy, with the challenge coming from understanding and controlling those factors affecting robustness. Developing these complex systems requires a good understanding of all factors and systematic testing.

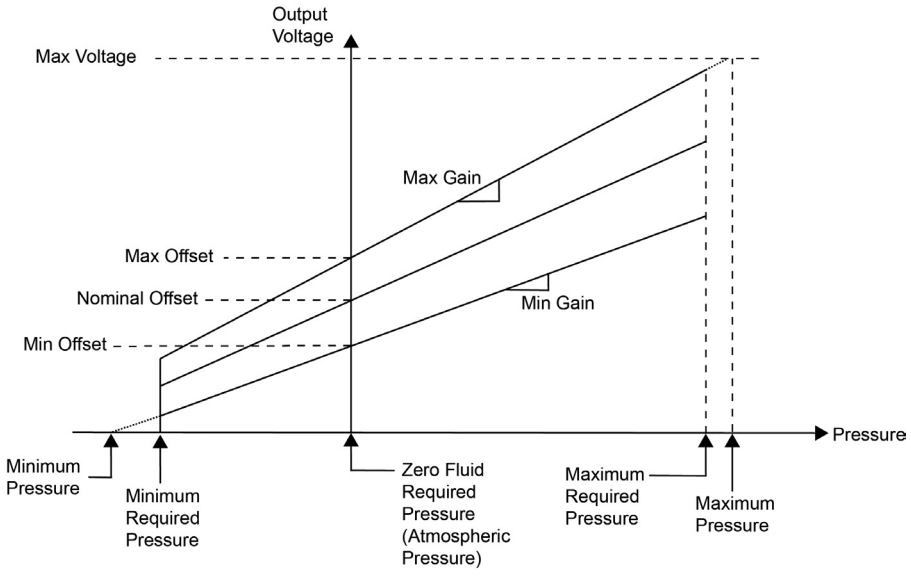

Figure 3: How the output voltage of a typical force sensor relates to pressure in the tubing set. This calculation would be performed by the infusion pump software and used to control certain occlusion alarm conditions. The force sensor can also be used to detect whether the disposable part is fitted correctly.

CONCLUSION

The technical issues outlined here are those which most commonly catch out first-time infusion pump designers. Each is

enough by itself to make an infusion pump unusable, either for safety concerns or for an abundance of nuisance alarms. These issues must be considered very early in the design process, and an approach must be taken that anticipates failure. Similarly, the stringent regulation of these devices warrants early consideration. Indeed, if these concerns are thoroughly understood, there are proven ways to design effective infusion devices.

ABOUT THE COMPANY

Sagentia is a global science, product and technology development consulting company that helps its clients maximise the value of their investments in R&D. Sagentia partners with clients in the medical, consumer and industrial sectors to help them understand the technology and market landscape, decide future strategy, solve complex science and technology challenges and deliver commercially successful products. Sagentia employs over 150 scientists, engineers and market experts and is a Science Group company. Science Group provides independent advisory and leading-edge product development services focused on science and technology initiatives. It has 16 European and North American offices, two UK-based, dedicated R&D innovation centres and more than 400 employees. Other Science Group companies include Leatherhead Food Research, TSG Consulting, Oakland Innovation and OTM Consulting.

BIBLIOGRAPHY

- *"BS EN 60601-2-24: Medical electrical equipment, Particular requirements for the basic safety and essential performance of infusion pumps and controllers". BSI, 2015.*
- *"Infusion Systems". MHRA, Dec 2013.*

ABOUT THE AUTHORS

Charlotte Harvey is a Medical Sector Manager at Sagentia. Her experience lies predominantly in managing medical product developments, specifically those in the surgical and drug delivery fields. Her recent projects have included investigating next generation infusion pumps, user interviewing for human factors, and several instances of developing reconstitution-based autoinjectors. Ms Harvey graduated from the University of Cambridge (UK) with a Masters in Mechanical Engineering.

Tim Frearson is a senior consultant at Sagentia. He has over 16 years of experience in medical device development. During his career he has been responsible for the design of electromechanical systems for intravenous drug delivery devices, has led Operational Excellence Lean Six Sigma process improvement projects focused within R&D and manufacturing, and project managed the next generation platform for a major infusion pump manufacturer in the US. Today, his focus is on delivering complex medical device development programmes for Sagentia's clients.