

# Death to the process

insight.  
ISSUE No.5

What factors influence, encourage, contribute to, and define what innovation is?



## IN THIS ISSUE

### ISO20072: the device developer's perspective

Max Middleton and Jamie Greenwood answer some frequently asked questions on the contentious standard.

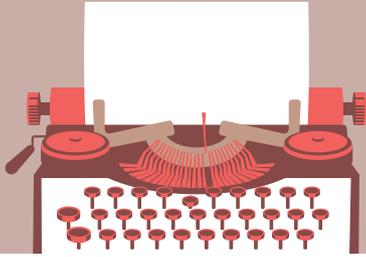
### Targeting the \$100 genome

Ben Wicks looks at the possibilities opened up through the speed of sequencing

### The usability of usability

Rob Fernall invents a simple game to highlight the challenges of terminology

# 04



## TARGETING THE \$100 GENOME

10 years ago the first human genome was sequenced and it took 13 years to do it. Today a human genome can be sequenced in just over an hour. Ben Wicks looks at what this means.

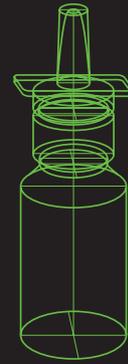
# 10



## HOW FAR SHOULD WE IMMERSE OURSELVES?

Team's Chairman, Jerry Turner, looks back at an early lesson in his career and asks how far we could and should go in order to put ourselves in the position of the user.

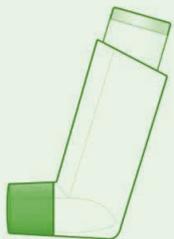
# 16



## DON'T TURN YOUR NOSE UP AT NASAL DELIVERY!

Andy Fry sniffs out (sorry) the focal points where nasal delivery has something to offer and why it might be better than the alternative.

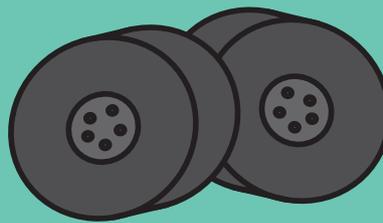
# 06



## ISO20072: THE DEVICE DEVELOPER'S PERSPECTIVE

Attempting to answer key questions around the relatively new ISO20072 standard and what it means in practice, Max Middleton and Jamie Greenwood provide a view from the front line of device development.

# 12



## INNOVATION IS...

You can't write a process for innovation. Instead Charlotte Clark and Paul Greenhalgh argue that it comes down to influencing, contributing and encouraging ideas through a range of factors, which they highlight.

# 20

## THE USABILITY OF USABILITY

# 22

## SELECTING MATERIALS FOR MEDICAL DEVICES

When developing a medical device, selecting the right material for each part is fundamental, and it demands an understanding of issues ranging from physical performance to supply chain logistics.

# 26



## MULTIPLE PERSONALITIES

Sophie Raven considers the multiple personality traits a good project manager needs to make sure projects run on time, keep to budget and meet the brief.

### Credits

**Editorial team:**  
Neil Cooper / Angela Murray  
**Designed by:** The District

Team / insight.

02 — 03

# It's all in the detail

BY **DAN FLICOS**

A recent documentary on man's mission to the moon featured the famous quote from JFK: "We choose to go to the moon in this decade and do the other things, not because they are easy, but because they are hard." Whilst we have no plans to start developing spacecraft, we believe that the advancement of medical science requires similar levels of vision and commitment. In this issue of Insight we reflect on the impact of cracking the human genome and where this might yet lead.

We also offer plenty of food for thought: What has deep sea diving got to do with medical device development? Why might a yoga teacher make a good project manager? Are noses overlooked? What does ISO20072 mean for you? What has the Devil got to do with material selection? How can we innovate in a regulated industry? Is usability usable? If this has piqued your interest, please read on to see what we think and whether you agree!

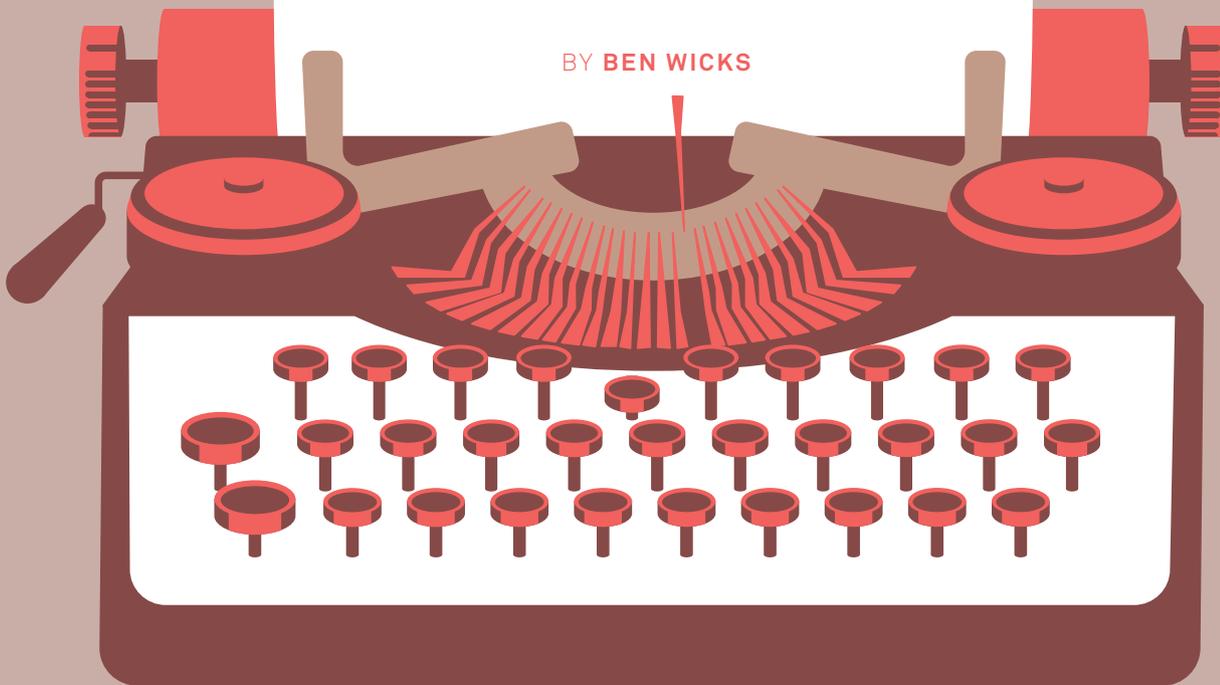
A handwritten signature in black ink that reads "Dan".

→ [dan.flicos@team-consulting.com](mailto:dan.flicos@team-consulting.com)  
*Dan is the CEO at Team and oversees the company's business strategy, client relationships and commercial opportunities.*

 **team.** | medical design and development

# Targeting the \$100 genome

BY BEN WICKS



Just round the corner from Team's offices is the Wellcome Trust Sanger Institute – one of the world's leading DNA research centres. The Sanger Institute played a key role in sequencing the first human genome which was completed in April 2003. It had taken the Sanger Institute, together with several other large centres around the world, over 13 years to sequence the 3.3 billion pairs of nucleotides in the human genome. Standing in the Sanger Institute's sequencing unit today it's hard to believe that the machines in front of me can now sequence a genome in just over an hour, 100,000 times faster than the first time.

The vast improvement in sequencing speed is partly due to the streamlining and optimisation of the 1st Gen sequencing technology which was

invented by double Nobel Laureate Frederick Sanger, here in Cambridge during the late 1970s. It is also due to the emergence of even higher throughput 'next generation sequencing' (NGS) technologies.

Before looking at NGS, let's recap how sequencing has been done up until now. Remember, DNA is just a long string of characters (A,T,C or G) so for the sake of this analogy let's imagine we want to know the sequence of letters in a piece of written text – let's say the first page of 'War and Peace'.

To work out the sequence of letters, imagine we type out page one over and over again using an old mechanical typewriter. We've deliberately modified the 'T' key so that it sometimes jams

the whole typewriter. Each time the typewriter jams, the partially completed page is removed and we start typing again on a blank sheet of paper. We end up with thousands of pages containing partially completed lengths of text of varying lengths, each always ending with a T.

To work out where the T's occur in the text we just need to count the numbers of letters typed onto each page. Some pages will have 46 characters because the typewriter jammed at the first T (which is the 46th character). Other pages will have 57, 59, 66 letters and so forth. By looking at the lengths of text generated, we can deduce the position of every letter T. By modifying the typewriter to jam at a different letters, then repeating the exercise, we can work out where each letter occurs in the sequence.

This is exactly how first generation sequencing works. The DNA sequence is copied billions of times by a DNA copying enzyme which occasionally gets jammed at a particular letter (known as a 'base'). By measuring the lengths of DNA strands which are produced you can work out the location of that particular base in the DNA sequence. You have to repeat the reaction for each of the four DNA bases (A,T,C and G) to elucidate the complete sequence.

The machines for doing this type of sequencing have got faster, cheaper and more accurate over the last decade but the approach is fundamentally limited in its throughput. Hence, scientists have been working hard to develop new approaches which can sequence DNA even faster.

## RAPID SEQUENCING WOULD ALLOW THE GENETIC COMPOSITION OF THE CELLS TO BE CHECKED BEFORE THEY ARE INJECTED INTO A PATIENT.

NGS technologies also use a DNA copying enzyme but rather than terminating the growing DNA strands and analysing them, NGS detects each time a new base is added to the growing strand of DNA. There are various ways of achieving this but most NGS technologies measure a fluorescence or electrochemical change brought about by the addition of a new base. It is difficult to overstate the magnitude of the technical challenge involved in this approach. Effectively you need to detect the addition of individual molecules to a DNA strand which is growing at around 1,000 new bases per second.

### The impact of NGS on healthcare

A huge amount of R&D resource has been invested in NGS technologies because the rewards are potentially enormous.

At the present time it costs around \$1,000 to sequence a person's genome. As the cost approaches \$100 per genome, the volume of commercial sequencing is set to increase exponentially as it becomes routine practice to sequence each patient's DNA. At this point, the availability of genetic information will begin to have a noticeable impact on healthcare.

Some of the impacts of low cost sequencing have already been well documented. For example:

- The potential of personalised medicine (selecting drugs for each patient based on their genetic profile) has been talked about for several decades and is already being used but will become more widespread as NGS takes off. It should also help pharmaceutical companies to revive some drugs which had previously been dropped due to patient genetic variability within clinical trials.
- Healthcare providers, payers and IT service providers are already beginning to think about the ethical, logistical and infrastructure issues created by the proliferation of all this genetic information.
- The practice of clinical microbiology will be transformed by the ability to routinely analyse the genetic composition of all isolates and to determine phenotype, in particular antibiotic sensitivity.

### Using NGS in cell therapy quality control

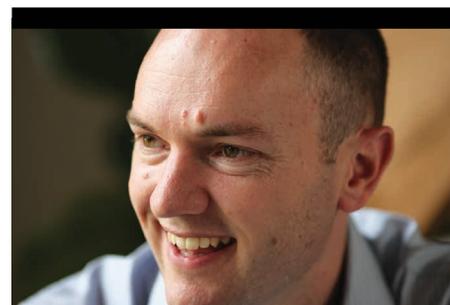
With all the fuss about personalised medicine, insurance, ethical questions and data integrity, I think that the impact of NGS on cell therapy may have been slightly overlooked. Research in cell therapy is progressing rapidly, yet the routine use of cells as therapeutics poses some particular challenges in terms of quality control which NGS could potentially solve.

Quality Control (QC) is a central pillar of drug safety. The pharmaceutical industry has applied stringent QC to chemical drugs for many years. Biologic drugs presented the pharma industry with a slightly bigger challenge, but proteins can now be

characterised with great precision. Cells, on the other hand, present a much greater QC challenge. The trouble with cells is that they grow, they change, they die, they aren't always identical and they may even mutate when you're not looking. Obviously, the biggest concern is that cells mutate and become cancerous. This is where rapid, cheap genome sequencing could be tremendously powerful. NGS would allow a sample of therapeutic cells to be sequenced quickly and accurately and be used as a release method for each batch.

Rapid sequencing would allow the genetic composition of the cells to be documented and checked before they are injected or infused into a patient. Quality Control perhaps isn't something which laboratory research scientists would necessarily be worried about, but regulators such as the FDA will demand a rigorous QC process before any cells are allowed to be used therapeutically.

Twenty five years ago everybody knew that mobile telephony would have a huge impact on society and communication. However, few could foresee the emergence of social media and its commercial and social impacts. I think there are parallels with NGS. We know it will change the nature of healthcare and we've identified some likely areas in which its impact will be felt. However, NGS will inevitably find new applications and enable technologies which we currently can't predict. Cell therapy may be one part of that future but we'll have to wait and see what else is in store.



→ [ben.wicks@team-consulting.com](mailto:ben.wicks@team-consulting.com)  
Ben is Head of Critical Care at Team Consulting. Before moving into the world of medical devices he used to be a molecular biologist and biochemist.

---

Team / insight.

BS EN ISO20072:2009 is a relatively new standard covering the vast majority of inhalers, which the standard refers to as ADDDs (aerosol drug delivery devices). While it is never mandatory to comply with a standard, it is generally thought to be 'highly advisable' to attempt to adhere to this one. Ignoring a standard where one exists can lead to awkward questions during the submission process, and within the industry as adherence to ISO20072 'will likely be necessary for manufacturers seeking approval to market inhaler devices in the European Union (EU)...[and] the FDA has expressed support in general terms for the ISO process' (Mitchell & Nerbrink, August 2012, 25(4))<sup>1</sup>.

BY MAX MIDDLETON & JAMIE GREENWOOD

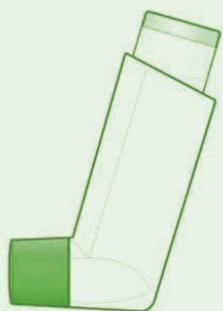
# ISO20072: the device developer's perspective

---

This standard is part of the 'risk based' approach to design verification that is becoming more and more important in medical device design. Although some aspects of the described testing are mandatory, the standard provides far more flexibility for developers to dictate what and how they test. As ever, this relies on developers to justify their decisions.

The standard is also intended to separately verify device performance outside of the wider pharmaceutical testing for combination product performance. This has led to a significant amount of confusion within the industry and some highly vocal criticism of the standard, as can be read in the IPAC/EPAG document<sup>2</sup>.

This article is a view from the 'front line' of device development, and attempts to answer these key questions honestly and practically. The answers may not solve all your problems - and may even conflict with other experts - but this is always the case when a standard continues to 'bed in' and there is no industry consensus on how best to interpret it.



## Q

### What is the Device Functionality Profile (DFP)?

## A

The standard describes the DFP (Device Functionality Profile) as being 'based on the outcome of the risk assessment'. We have found it more useful to consider the DFP as a statement of what your device needs to do in order to 'work'. After all, the risk assessment is an analysis of how the device might not 'work'.

Because of this, the DFP has only an oblique relationship with the product requirements. Important success criteria will probably be duplicated, such as the maximum user forces, but important component interactions and device states are also likely to be included. The bottom line is: if you can confirm that all items in the DFP have been achieved (either yes/no or within an acceptable range) the device should be ready to emit its dose in the correct fashion.

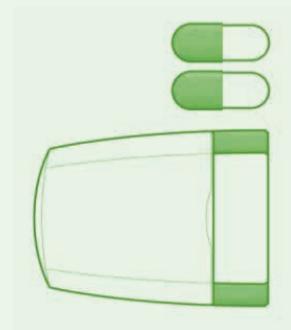
## Q

### What about the relationship of the DFP with the risk assessments?

## A

There are two key ways in which the DFP interacts with the risk assessments:

- New functions (possibly unexpected, unwanted functions), or critical component states can be discovered within the risk assessment and added to the DFP. For instance, you could state in the DFP that an actuation lever must not be capable of being rotated into a discovered incorrect position.
- New pre-conditions can be uncovered in the risk assessment and added to the list of tests. Two common examples would be compression tests (on the assumption that your customer treads or sits on the device) and 'bulk transport tests', which are not in the standard, but which regularly appear in risk assessments.



## Q

### What about the relationship of the DFP with pharmaceutical testing?

## A

The device-only functions described above are relatively straightforward to plan for. However, the standard also states that the DFP should include a 'system verification test', which 'comprises either emitted mass or dose testing, as determined from the risk assessment'. This should be expected as, after all, the primary function of the device is to deliver the correct dose. This section in particular has led to much of the confusion with - and potential rejection of - the standard as it intrudes directly into the already prescribed practices for pharmaceutical performance testing of the product<sup>2</sup>.

Although it may be considered to be dodging the issue, we have generally found that this part of the standard should be left out of the device verification programme completely until the contradiction is resolved in later versions. Justification can be drafted that pharmaceutical testing of the product is carried out separately and that it covers this aspect of the standard.

**Q**

**Do all the device functions need to be in the DFP?**

**A**

Due to the link to the risk assessments, all functions that are critical to the operation of the device should be included in the DFP. If the risk assessment shows that there is no unacceptable harm from a function failing, then the function need not be tested.

However, the justification for excluding a function will need to be carefully considered. We have found it more common to want to exclude functions that are likely to fail under the environmental pre-conditions (see more below). While understandable, this requires the development team to justify that the function is not critical.

**Q**

**Why are the environmental conditions so tough...what about electronics?**

**A**

Although not particularly well documented, the intention of the standard is that you test the device in relation to the environmental limits of the label claim for the product. The stated conditions are included as a guide if the developer has yet to define the label claims.

However, although testing to the label claim is a good starting point, based on the standard's link to the risk assessment, it is likely that the developer will need to test the device at a wider range of temperatures than the label claim states. It may be considered an acceptable risk to receive a low dose after the inhaler has been left on the apocryphal 'dashboard in a car in Florida', but it won't be an acceptable risk if the device could lock up completely, thereby permanently ceasing to function.

We have found that electronics pose a particular challenge for adherence to ISO20072. Moving the device from hot, humid conditions to cold, dry conditions — and back again — can lead to internal condensation and failure of these electronic functions. This is especially true where devices have been designed before ISO20072 was released.

**Q**

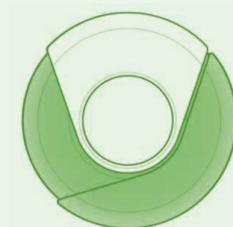
**How does one control the test environment to the required accuracy for these tests?**

**A**

The standard states that 'unless otherwise specified, test measurements shall be performed at standard atmospheric conditions', which are 25degC at 60% RH with relatively tight tolerances ( $\pm 2$ degC and 5% RH). The design team needs to think about the ability of the test facility to reliably maintain these conditions for, potentially, a number of months for a typical ADDD verification programme. This presents a real challenge for the climate control (and monitoring) capabilities of the proposed test facility, and covers many aspects of laboratory climate control including:

- Uniformity of the atmosphere across the lab - the prevention of 'tropical hot-spots' for example, or whether there is a good distribution of humidified air throughout the lab (rather than just a humidification 'loop' in the region of the humidifier).
- The lab design, particularly with air exchange with the outside – the effect of when the lab doors open due to operator traffic, for example, and how well sealed the lab is to prevent leakage around windows, doors, light fittings and so on.
- Many modern labs have extracting fume hoods which can make climate control even more challenging. If any aspects of DFP assessment require the use of a fume hood, then the design of the room and climate control system needs to be able to compensate for the volume of air being extracted from the room.

It is fair to say that a combination of these factors makes the maintenance of the required test environment incredibly challenging for many laboratories, especially those built to maintain environmental conditions set according to much less stringent boundaries (such as ISO11608 for liquid-based pen injector systems). Remedying this discrepancy potentially requires a great deal of investment in the test facility.



**Q**

**How does one verify the function of internal mechanisms that are not visible?**

**A**

This is a difficult question and the answer will depend on the device. We have solved the problem in two separate ways:

- You can modify the device so that the mechanism can be seen (through the use of clear materials on case-work parts, or cut-aways). You will need to justify why these modifications do not affect the results of the verification testing.
- You can imply the successful operation of the mechanism through its end effect, and by considering what observable effect may occur if the mechanism does not function. If the only observable effect is dose accuracy, you may have to ensure that the operation of the mechanism is tested adequately in the pharmaceutical testing, further complicating the link between the device testing and the pharmaceutical testing.

Q

**How many devices do I need to test?**

A

As with any statistical methodology, there is no 'correct' answer to this. The key factor is whether you are able to have

measurable 'variable' results from the test, or if you have pass/fail 'discrete' results. If you can construct the DFP to specify 'variable' results, you should be able to use sample sizes of 20-30 and achieve suitable data. If you have 'discrete' results, you will need sample sizes of 200-300 to achieve a similar level of confidence in the results.

Even though it is not mandatory to only have 'variable' or 'discrete' tests, you should typically try to have tests of all one type. If you have any 'discrete' results you will need to test hundreds of devices, but 'variable' results are typically more challenging and take more time to measure. If you are forced into a large sample size because of one particular 'discrete' result, this can lead to a very long (and expensive) test programme.

The variability of the test procedure is an important factor when deciding how many devices to test. The standard uses 'k-factors' to modify the acceptance criteria in the DFP to be valid for the test sample size. If a smaller sample size is selected, the standard effectively requires you to show a much smaller variation in results to be deemed acceptable. Smaller sample sizes may be shown to fail due to variation in the test, rather than the device. In this type of situation, Measurement Systems Analysis (or similar techniques) should be used as early as possible to determine the variability in apparatus and operator that you will need to account for by potentially increasing sample size.

As with any statistical methodology, there is no 'correct' answer

Q

**How does one deal with the requirements of the standard that are not part of the DFP test?**

A

Sections 5.1 and 8 of the standard appear only to be related to the bulk of the described tests by merit of their inclusion in the same document. They include other, more general requirements for the device, and as such are a mix of specific device requirements (such as remaining dose indication), and requirements more closely related to the complete product (such as secondary packaging markings), and to the product development (such as justification for material selection).

These sections have an uncertain relationship with the DFP aspect of the standard. Some of the requirements (such as dose indication) are likely to form part of the DFP, unless you can justify why accurate dose indication is not critical functionality and has no associated risks. Some requirements only indicate the recommended standard for software or electronic testing and risk complicating the developer's validation documentation.

In addition, several required areas (such as the IFU content) are likely to be completed after design verification.

Because of these factors, we have generally recommended that the majority of these requirements can be covered in a properly planned and documented project review after completion of the DFP testing, and in isolation from it. This allows the developers to 'tick off' that they have met these additional requirements with the minimum of cost.



→ [max.middleton@team-consulting.com](mailto:max.middleton@team-consulting.com)  
Max Middleton is a senior project manager and has recently completed a programme to carry out the design verification of an inhaler, focusing particularly on the design of the verification programme and the fit of the standard within it.



→ [jamie.greenwood@team-consulting.com](mailto:jamie.greenwood@team-consulting.com)  
Jamie Greenwood is Team Consulting's laboratory manager. He recently led the design verification of an inhaler, focusing particularly on the design of the test programme and the management of the facilities needed to achieve the testing required.

#### References

1. Mitchell, J P, Nerbrink, O, Comparison of ISO Standards for Device Performance; 20072 and 27427: A Critical Appraisal, *Journal of Aerosol Medicine and Pulmonary Drug Delivery*, August 2012, 25(4), pp209-216.
2. International Pharmaceutical Aerosol Consortium on Regulation and Science (IPAC) and European Pharmaceutical Aerosol Group (EPAG), Justification of the Request for a Negative Vote on ISO DIS 20072, *Aerosol Drug Delivery Device Design Verification – Requirements and Methods*, 2008.

# HOW FAR SHOULD WE IMMERSE OURSELVES?

BY JERRY TURNER

In 1973 I qualified in Mechanical Engineering Design from The Polytechnic of the South Bank and went into full-time employment with a cable making company, designing and developing cable making machinery. Pretty boring stuff actually! The extent of human interface design was usually a simple control box with large start and stop buttons, an even larger emergency stop button, and perhaps a speed control of some description. When designing a machine, very little attention was paid to what we now call Human Factors Engineering.



After five years I'd had enough and I moved to a UK company which developed and sold products to the global offshore oil and gas industry - everything from non-destructive test equipment to one-man atmospheric submersibles and remotely operated underwater vehicles. In those days it was a really exciting and dynamic industry – pioneering in fact.

So there I was; five years of experience and I thought I could design pretty much anything. When I was asked to design an underwater ultra-violet lamp I thought "That's not hard. No problem". The lamp was one element of a non-destructive testing system which could detect surface-breaking cracks in the steel of offshore structures by employing a technique known as Magnetic Particle Inspection (MPI). I got on with the task, sourced a UV emitting bulb (the sort which were in those - now very old fashioned - UV lamps that some people used for tanning), a glass 'black light' filter because the emitted UV needed to be of a particular wavelength, an underwater electrical connector and a few other bits and pieces. All that remained was to design the waterproof housing. It had to withstand the pressure at a depth of 140 metres with a safety factor of 2:1.

What with the size of the lamp and the thickness of the housing it ended up as quite a heavy and bulky piece of kit. I had it made in our own workshop, pressure tested it and gave it to our staff diver and submersible pilot, Paul, to test.

"What's this?" he asked. I told him. "Absolutely hopeless!" he exclaimed and threw it over his shoulder. "Have you ever dived?" he asked. I hadn't. "What you need to understand is that a commercial diver can use, at most, just 10 per cent of his concentration on carrying out the task in hand. Ninety percent of his concentration is focused on staying alive. It's a very hostile and difficult environment down there, so he needs equipment which is very easy to use and is as light and as small as possible."

He went on to paint a picture of what it was like to work as a commercial diver and I began to understand.

The Mk 2 UV lamp was designed and made. This time Paul said: "Better, but still a way to go," and then, "come with me, I'm going to teach you to dive."

The dive-tank was outside and open to the elements. It was January, there was a light covering of snow on the ground and about an inch of ice on the surface of the water in the tank. He put me in a wetsuit and typical sport diving gear. We broke up the ice and I tried to get into the water down the access ladder. I managed to get in as far as chest height before hyperventilating, so I climbed out, shivering and numb. Paul admitted it had been an unfair but deliberately shocking experience "...to get your attention." It worked!

## "COME WITH ME, I'M GOING TO TEACH YOU TO DIVE"

Over the next six weeks or so he put me through an intensive diver training course, the theory and practice of which would be familiar to sport divers, and then on to experience (as far as was practically possible) some typical tasks a commercial diver has to undertake by simulating the conditions found offshore at different depths whilst using the equipment a commercial diver uses.

Why am I recounting this story from over 30 years ago? Because it made it clear to me early in my career that we need to put ourselves in the shoes (or diving suit!) of the users of our products to get a clearer understanding of what life is like for them and the context of use. This is difficult when it comes to medical devices. We can't and shouldn't test auto-injectors on ourselves. We can't use the intern for in-house surgical procedures or remove the liver from the office manager. Instead we have to empathise.

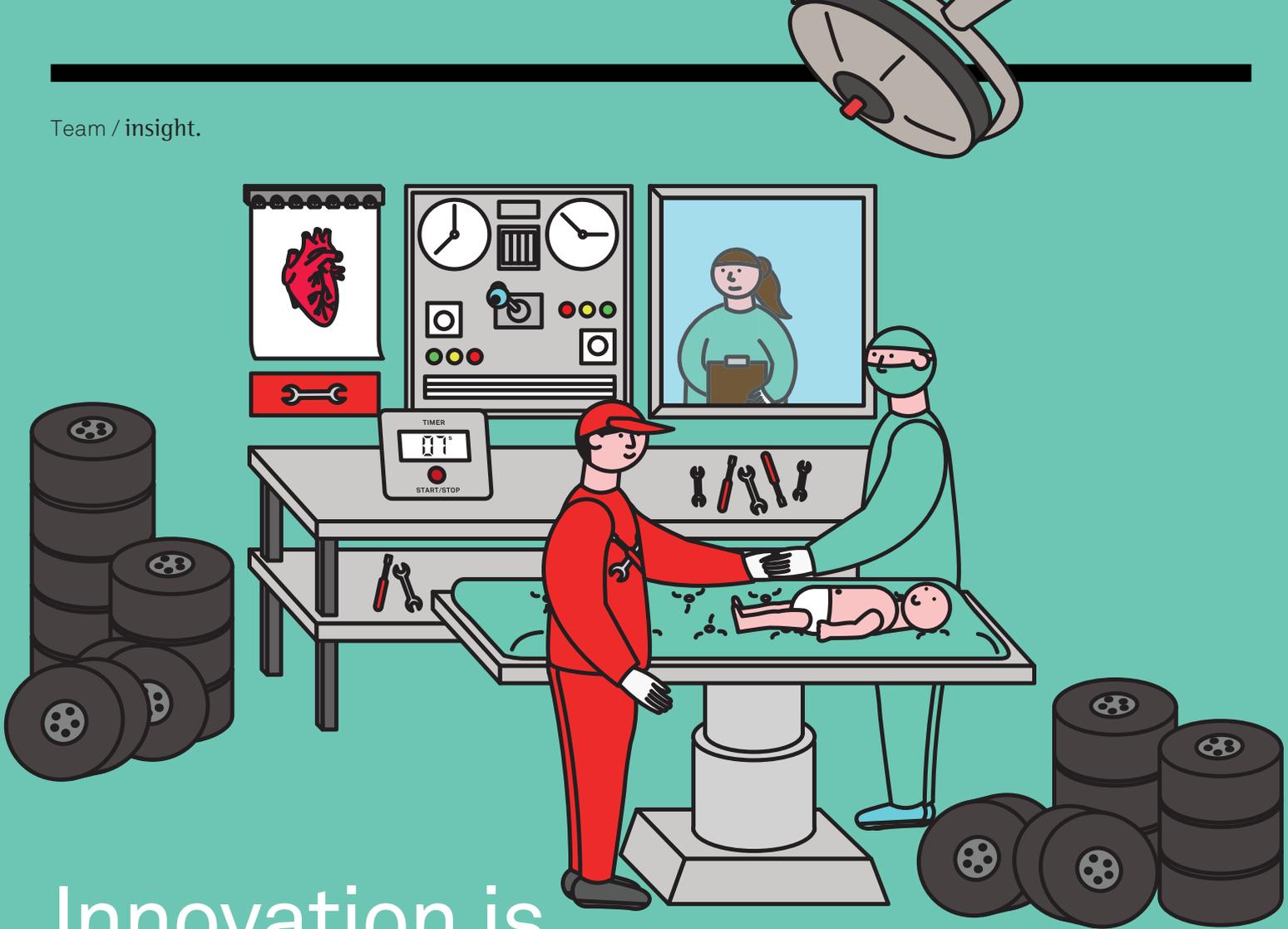
There are lots of different characteristics that come together to create the culture at Team. Attention to detail, the importance of relationships, and so on. But empathy is one of these too. When we are face-to-face with users during usability testing, we empathise with them and with what can be a really stressful and emotionally draining situation. Our designers talk to users and try and understand their world, and the engineers think about the patient during product development: can they operate it, does their condition make it difficult to hold it, is it too heavy, how often will it be used, does it need to withstand life at the bottom of a sports bag or handbag?

We work for our clients, and delivering value to them is of paramount concern, but so is the user's experience. We can't separate the client and user. The product has to be commercially viable but it will also have to save a life or make life better. This doesn't cause conflict, just challenges.

What about the UV lamp development? The Mk 3 version was very successful in the market and a derivative of it is still in use today.



→ [jerry.turner@team-consulting.com](mailto:jerry.turner@team-consulting.com)  
Jerry joined Team in 1991 and became CEO shortly afterwards, a role that he continued to hold until 2012 when he moved into the Chairman role.



# Innovation is...

BY PAUL GREENHALGH & CHARLOTTE CLARK

You'd be excused for thinking that innovation is challenging, especially in the medical devices sector, a rigorously regulated environment, dominated by process and the need to assess and mitigate risk. It's not the most nurturing environment for brave new ideas so who could blame some companies for seeing these obstacles as an excuse to stay safe, only evolving products 'little by little' when there is real evidence to do so.

But staying safe could be fatal in an ever-changing world. Web savvy patients are becoming more empowered, pressure is on to reduce healthcare costs, blockbuster drugs are coming 'off patent', budgets are restricted, regulations are evolving, and new technologies are constantly emerging – how do you innovate to keep ahead of the competition?

As product developers in the medical sector, it's easy to think of innovation as another process that needs defining. But to see it that way could be detrimental to success, as Sir George Buckley, CEO of 3M, said recently: "When we started to define an innovation process it was some of the darkest times at 3M."

So if innovation is not a process — what is it? We prefer to think of it as 'a state of mind'. Sure, not everyone is naturally 'innovative' - and some people are far better at it than others - but with the right mind-set, a good toolkit, a mix of people to collaborate with and a nurturing environment, most people could have a damn good go. So how can you lay the foundations to allow innovation to flourish?

There are many influencing factors that can encourage good innovation and it's often a combination of these which help

to spark creativity and ultimately lead to success. These factors are applicable, not just in the medical device sector, but in many other fields and we can, and should, learn from innovations occurring in industries outside of our own.

---

**SO IF INNOVATION IS NOT A PROCESS — WHAT IS IT? WE PREFER TO THINK OF IT AS 'A STATE OF MIND'.**

---

Here are 10 different factors which we believe will influence, encourage, contribute to, and help define what innovation is, whatever field you work in:

## ALL IN THE MIND

“We can’t solve problems by using the same kind of thinking we used when we created them.”

Albert Einstein

Innovation is about mind-set, about training your brain to think and see things differently and constantly asking ‘why..?’, ‘how’ and ‘what if..?’. It’s not just thinking outside the box - but tearing it up and trying something else altogether. As Christian Rangen of Engage//Innovate commented it’s about encouraging a range of more open mind-sets, from ‘dreaming bigger’ to ‘pirate thinking’.

## ABOUT INSPIRING

“All the effort in the world won't matter if you're not inspired.”

Chuck Palahniuk

In order to innovate you need to inspire. Red Bull is one example of a truly inspirational company. It was started in 1987 by Austrian entrepreneur Dietrich Mateschitz who was inspired by a pre-existing Thai energy drink named Krating Daeng. He had a vision for the product, created Red Bull, and then set about creating innovative ways to increase global brand awareness. Red Bull is now snapping at the heels of Pepsi and Coca Cola; it has become one of the world’s most popular drinks, with two teams in Formula One, and has re-written the rule book on how to sell a product by focusing on the drink’s energy-giving properties while projecting an edgy, high-adrenaline image. This has been achieved by events and activities ranging from support for spinal-injury research to sponsoring Felix Baumgartner’s free fall from the edge of space. We can learn a lot about how to inspire people to ‘think differently’ from companies like Red Bull.

## FOR PEOPLE

“If we’d asked people what they’d wanted, they would have said ‘faster horses!’”

Henry Ford

When innovating new strategies, ideas and products, especially in a sector such as medical, it is crucial to keep all relevant stakeholders at the forefront of your mind – from patients and health care professionals to hospital porters. In what can be a highly stressful and risky environment, the needs of those for whom you are innovating are of utmost importance and are often the source of innovative ideas.

One problem, however, is that people don’t often know what they want until you show it to them. Innovation using standard market research techniques, such as focus groups, can therefore be tricky as people can only tell you about what they know right now. Successful innovations anticipate what’s on the horizon and second guess what people will want in the future.

In the medical sector, patients are becoming more empowered and increasingly act just as any other consumer. They consider their medical devices in the context of the other products which surround them, so macro product trends and trends affecting other industries need to be considered. Even the passive term ‘patient’ may soon become outdated. Some techniques, such as design research, can deliver valuable insights into the contexts and scenarios in which people function - now, and possibly in the future - thereby uncovering needs that these very same people would not be able to tell you they had.

One clinic in Massachusetts has set up an innovative "Walking in the Patient's Footsteps" programme which shadows patients throughout their health care experience. Students play a major role in the program as the clinic has found that students can be invaluable observers and listeners in ways that more experienced professionals cannot. As a result, some of the clinic’s best innovations have come from students making observations that other doctors did not.



## BY PEOPLE

“Many ideas grow better when transplanted into another mind than the one where they sprang up.”

Oliver Wendell Holmes

Ultimately, innovation comes from people; people talking, or people with different backgrounds and skills, sharing ideas and experiences. Whether it’s a chance meeting over the coffee machine, a more formal creative session, or on a much bigger scale like crowdsourcing – collaboration allows people to bounce ideas around and build on ideas and experiences of others. Take Great Ormond Street Hospital. The neonatal cardiac surgery success rate was lower than expected and they couldn’t work out why. Investigation showed inconsistencies in the handover procedure between the theatre and neonatal unit. Inspired by the co-ordination, discipline and ability of Formula One pit stop crews to seamlessly service a car in seven seconds flat, doctors collaborated with McLaren and Ferrari managers, and an industrial psychologist, to completely transform the surgery handover process. This team of people with different backgrounds and experiences learnt from each other, implementing a change which directly saved the lives of many babies.

## ABOUT A STIMULATING ENVIRONMENT

“[to encourage innovation]... create a highly engaging work environment that inspires employees to give the very best of themselves.”

Gary Hamel

It's no secret that the working environment contributes to overall happiness and creativity. Simple things such as specific zones for working, creation, relaxation and play, colour, improved lighting and ventilation, and food and drink, can all dramatically improve creativity. A free-flow environment, with 'hot desking' for some employees, can encourage movement around the office, increasing the chance of different people talking together, collaborating, sharing and bouncing ideas of each other. Moving away from seating by 'sector' and mixing staff from different disciplines, and from an environment where furniture is permanent to a space which is easier to rearrange and evolve, can significantly affect the way teams interact. These, along with visual stimulation, such as inspirational quotes and exciting objects and images, all help to get the creative juices flowing. Even taking teams outside their normal working environment can have a dramatic effect on levels of creativity.

High-tech giant Adobe recently opened a striking new building in Lehi, Utah specifically designed to create an ecology of planned and unplanned cooperation and innovation among its employees. Eighty five per cent of the interior is open workspace - with only 15% devoted to offices. The building includes a full basketball court and extensive fitness areas, pool tables, a café and eating/lounging area — all to encourage employees to meet and interact with each other. Adobe hopes that by pushing employees out of their offices, they will run into each other more often, spontaneously generating ideas and solutions.

## ABOUT HAVING A GOOD TOOLBOX

“Anyone can look for fashion in a boutique or history in a museum. The creative explorer looks for history in a hardware store and fashion in an airport.”

Robert Wieder

Often the hardest part of generating innovative solutions is knowing where and how to look for them, and often inspiration comes from outside your own industry.

In the late 1990s, Medtronic scientist Ken Brennan was struggling to make pacemaker leads fit into the small veins on the left side of the heart. Ken's eureka moment came while reading a magazine article about a new material developed by NASA, designed to withstand the severe conditions in outer space – a technological advancement outside his own industry which would allow the leads to be much narrower.

In a recent development that we undertook at Team, we had to devise a way of protecting a transplantable human liver during transit. The inspiration for this came from a £5 rubber colander bought from a department store, and some plastic containers from the supermarket.

There are many creative tools out there, designed to help innovators define problems and then generate, filter and select or implement ideas – and all have their good and bad points. These create and innovation techniques can be likened to DIY tools in a toolbox, But whether you are using Lego, the innovation pyramid, analogous industries, MECE mapping, random associations or any other of the many tools available, the key to success is picking the right tool for the job.

## ABOUT WITH-HOLDING CRITICISM AND CONSTRAINTS... INITIALLY

“If at first an idea is not absurd then there is no hope for it.”

Albert Einstein

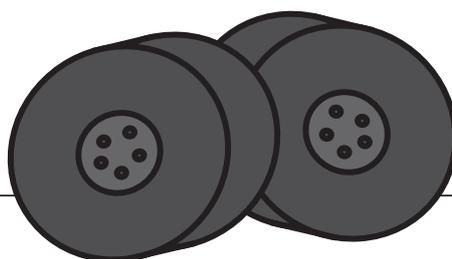
Enforcing artificial constraints can sometimes aid creativity, but in general, when coming up with ideas, withhold judgement and ignore all major commercial, regulatory and technological constraints initially and see what emerges – otherwise you might miss a great opportunity. As Lee de Forest said in 1926: “While theoretically television may be feasible, commercially and financially, I consider it an impossibility; a development of which we need waste little time dreaming”.

Focus idea creation on individual problems so that you are not overawed by the limitless possibilities, but once you've blown the ideas wide, add in constraints and selection criteria to help identify those that best satisfy your requirements. You may even find this a source of innovation itself! But at least you know you left no stone unturned.

---

**FOCUS IDEA  
CREATION ON  
INDIVIDUAL  
PROBLEMS RATHER  
THAN LIMITLESS  
POSSIBILITIES**

---



## ABOUT BEING PREPARED TO TAKE RISKS

“Whenever you see a successful business, someone made a courageous decision.”

Peter Drucker

Sometimes things don't work out and that's OK. We can learn from these mistakes and move on, but if you won't try something in the first place how will you know if you're sitting on the next big thing?

Amazon.com, now one of the world's largest online retailers, started as an online bookstore, but soon diversified into DVDs, VHSs, CDs, video and MP3 downloads/streaming, software, video games, electronics, apparel, furniture, food, toys and jewellery. Over the years Amazon has tried other less successful ventures, including selling mobile homes, but it hasn't stopped it looking at how it can use its resources to expand its business. As a result, Amazon is now also one of the largest providers of cloud computing services.

Novo Nordisk is another perfect example. In 1981, Novo was a pharmaceutical-chemical company manufacturing insulin which found anything mechanical far beyond its field of expertise. The Marketing Director had an idea for delivering incremental doses of insulin using a 'pen', instead of the standard syringe and vial. The company saw the potential for the product and developed a design inspired by well-known technologies including the switchboard, Leonardo Da Vinci's ship propeller and the collapsible Chaublin clasp nut. Without in house capabilities, and unable to find suitable production partners, Novo set up its own assembly plant and based production on parts made in Denmark, Germany and Switzerland – a big risk for a pharma-chemical company. Clinical studies showed improved control and that 90% of patients preferred the new type of delivery method. The gamble had paid off and the insulin pen was born.

Imagine how different things might have been for Kodak and Nokia if they had taken more risks. Kodak had the technology for the digital camera in 1973, and Nokia tried to launch an app store well before Apple, but both were thwarted by senior management. They both had the technology, but decision makers couldn't imagine it and weren't prepared to take the risk.

## GOOD DESIGN AND ENGINEERING

“Design is not just what it looks and feels like. Design is how it works.”

Steve Jobs

Creativity is thinking up new things; innovation is doing new things. For a really great idea to be realised, you need good design and engineering. Without either of these it simply won't work.

In 1978, James Dyson noticed how the air filter in the Ballbarrow spray-finishing room was constantly clogging with powder. To fix this, he designed and built an industrial cyclone tower which removed the powder particles by exerting centrifugal forces. He wondered if the same principle work in a vacuum cleaner, and five years and 5,127 prototypes later, the world's first bagless vacuum cleaner arrived. Without Dyson's persistence, some really good engineering and a great design, Dyson vacuum cleaners would not be as successful as they are today.

## ABOUT LEADING FROM THE TOP

“Who the hell wants to hear actors talk?”

HM Warner, Warner Brothers 1927

Lastly, and possibly most importantly, a successful innovation company has to have innovative leaders. If senior management doesn't have the right mind set then forget it. Look at Richard Branson... he's a prime

example of an innovative leader. He's not afraid to take risks and learns from his mistakes, moving onwards and upwards. If he had never crashed his hot air balloon would he now be commercialising space travel?

Innovation runs right through the Virgin organisation from top to bottom, with all employees encouraged to be part of the innovation process. One recent cost saving innovation came from a member of Virgin Atlantic's cabin crew whose idea was to pour the champagne in first class then offload the bottles before the planes took off, thus saving weight and making a minimal reduction in fuel costs. Multiply this saving by the number of flights taking off every day, and the other ideas that it might provoke, and you start to see that any idea, no matter how small can be a winner. Individuals, however, need to feel empowered to make suggestions - much more likely when top management are ambassadors for innovation.

So there you have it. These ten factors are just some of many which could be used to encourage creativity and successful innovation, and are among those we have found to be the most successful. The medical device industry will always be a challenging sector in which to innovate, and we know that different things work for different organisations, so we invite you to share your own ideas around innovation with us, especially what's worked for you (or not!) in your own organisations.



→ [charlotte.clark@team-consulting.com](mailto:charlotte.clark@team-consulting.com)  
 → [paul.greenhalgh@team-consulting.com](mailto:paul.greenhalgh@team-consulting.com)  
*Charlotte is a senior consultant, focused around the front end of the product development process. Paul is director of design and has led the design or programme management of many products.*

---

Team / insight.

# Don't turn your nose up at nasal delivery!

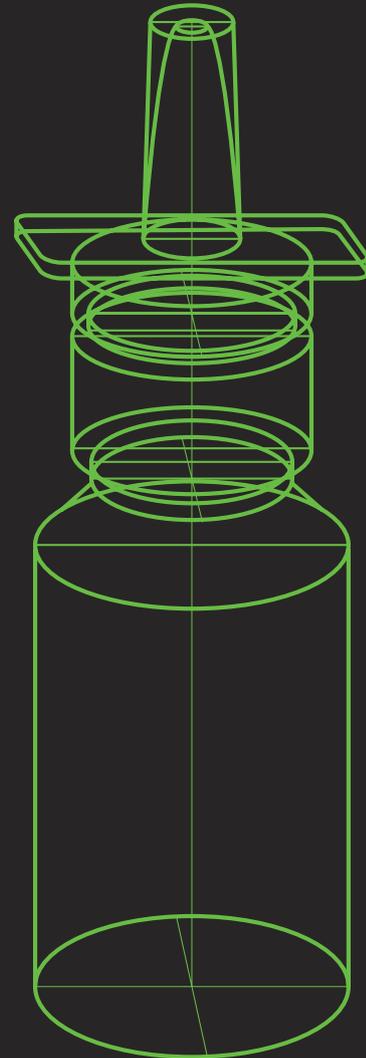
BY ANDY FRY

A survey carried out in 2003 by the Institute for Biomedical and Pharmaceutical Research in Nuremberg found that over 90% of Euro banknotes showed traces of cocaine.

In 2009, the University of Massachusetts reported similar findings for US banknotes. In both cases, the use of rolled-up banknotes to 'snort' lines of cocaine was given as the root cause for this contamination, though both studies acknowledged that transfer between notes in cash dispensing or note counting machines had exaggerated the extent of this 'recreational' use of currency. Although this variant of nasal delivery does not appear in any of the established pharmacopeia, these studies are a reminder that the nose is recognised as a very convenient portal

of administration for medications, whether or not formally prescribed. The indigenous peoples of North and South America were using nasal delivery for tobacco snuff and a variety of psychotropic herbal concoctions centuries ago. Indian and Persian records show that physicians and apothecaries were making widespread use of the nose to treat a range of conditions back in medieval times. In Europe and the USA, nasal delivery experienced a surge in interest from the 1980s onwards; as a result, over the past three decades some excellent

research, together with very innovative development in formulations and devices, has revealed significant opportunities in nasal delivery thereby generating substantial market growth by the turn of the century. Depending on which survey you read, the global nasal drug delivery market is now estimated at around \$8.5 Bn. Market growth for nasal products was running at around 20% annually at the turn of the century, though it is presently closer to 6%. Nasal delivery still has great promise, but we should also remain aware that nasal delivery is not without its challenges.



### WHY, WHAT, WHERE AND HOW?

Back in the early 1990s, I remember a senior figure from a major pharma roundly dismissing nasal delivery as “something for a runny nose and little else”. Given that Team were developing a successful nasal device for a hormone-based systemic therapy at the time, and had previously worked on a number of other innovative nasally-delivered therapies, I was somewhat indignant. However, for anyone operating outside those fields in which the nose presented a promising delivery route, the view expressed was perhaps understandable. Today there is a greater awareness of device-based drug delivery in general, and specifically of nasal delivery. So where are the focal points where nasal delivery has something to offer and why might it be any better than alternative, perhaps better understood routes of administration?

*The nose presents a large area of highly vascularised, accessible mucosa.*

### LET'S START WITH WHY

The nose presents a large area of highly vascularised, accessible mucosa. Delivery is non-invasive and avoids first-pass hepatic metabolism, with excellent bioavailability and rapid onset of action in many cases. Recognition of these attributes was a major factor in the rapid growth of nasally delivered drugs, especially in systemic applications, in the 1980s and 90s.

### SO WHAT CONDITIONS AND THERAPIES ARE SUITED TO THE NASAL ROUTE?

Runny noses are still a nuisance and to no great surprise, OTC decongestants and prescription allergy therapies still account for between 70 - 80% of the nasal market by value. Predominantly, this segment is about large volumes of low-priced products. The remainder of the market is comprised almost entirely of a range of prescription systemic therapies, with lower sales volumes but significantly higher priced products. Drugs and conditions treated include the following:

### Vaccines

The nasal mucosal lining provides an excellent site for vaccination. ‘FluMist®/Fluenz’ for influenza is licensed in the EU and USA and vaccines for a number of other diseases are under development, including influenza H1N1, Norovirus, and West Nile virus.

### Hormones

There is significant interest in nasal delivery of a range of hormones including parathyroid hormone (PTH), for treatment of osteoporosis, and human growth hormone (HGH). Results comparable to injected delivery are claimed for intranasal HGH.

### CNS

Sumatriptan, for migraine relief, was first introduced as a nasal spray by Glaxo in 1997, providing a rapid acting, needle-free alternative to injection. AstraZeneca introduced a nasal spray version of their Zolmitriptan migraine treatment in 2002.

### Breakthrough cancer pain

PecFent® was launched by Archimedes Pharma in 2010 as a nasally delivered spray of Fentanyl, a powerful opioid analgesic, formulated to gel in contact with the nasal mucosa, from where it is rapidly absorbed to provide relief.

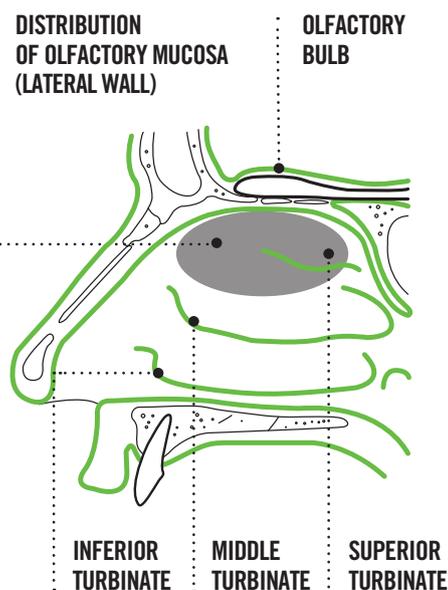
### Rescue medication

Nasally delivered Midazolam for treating epileptic seizures is simple, quick, involves no needles and has a very rapid onset. Results are encouraging and approval in the EU is expected shortly. Alternative delivery routes (IV or IM injection or rectal) involve needles, may be awkward to use, and have delayed onset.

### Heroin overdose

Another area for rescue treatment is that of heroin overdose. Naloxone, an opioid antagonist that reverses the effects of opioid overdose, has proved highly effective in a nasally delivered format, with similar advantages to those found in seizure rescue treatment.

As a generalisation, lipophilic drugs are more readily suited to nasal absorption than hydrophilic drugs, though formulations have been developed to compensate for poor absorption of the latter. Also, in terms of molecular weight, 1kDa is generally regarded as a practical cut-off, but once again, innovative formulations and enhancers have been developed to allow for delivery of larger molecules such as PTH, for instance, with a molecular weight of 4.18 kDa.



### AS TO WHERE?

Sure, we stick the medicine up the nose – is that it? Well no, not really. The nose is a complex organ. The anterior portion (the visible part) is largely lined with non-ciliated, squamous epithelium and is not the preferred site for drug delivery. For most systemic applications, the turbinates or concha, scroll-like features along the sides of the nasal passageways and covered with ciliated mucosal tissue, are where absorption mainly takes place. The olfactory region, in the ‘roof’ of the nasal cavity, is of key interest for CNS delivery; nerve fibres from the olfactory bulb (within the frontal brain) extend through a thin, perforated portion of the skull (the cribriform plate) to present a high density of olfactory receptor cells within the nasal cavity. These form a connection from nose to brain, bypassing the blood-brain barrier.

## FINALLY, HOW?

User technique and device design for maximum usability are one aspect of this topic, while getting the formulation right is the other. It is always best to consider formulation and device design at the same time, early on in the development of any combination product, but this is especially so in the case of nasal delivery. The range of devices and formulations available is extensive, so here are just a few top-level observations, principally relating to nasal sprays (the most common format compared to drops or gels):

*Sure, we stick the medicine up the nose – is that it?  
Well no, not really.*

### User technique and device design are not readily separated.

Ideally, spray performance should be operator independent – operating mechanisms which ‘trigger and deliver’ at a set force threshold are beneficial. Location within the nostril is clearly important – designs which encourage correct engagement in the nostril and maintain device position during actuation aid consistency. Innovative device technologies such as the Aerogen nasal mesh nebuliser, OptiNose Bi-directional nasal delivery system or Impel Neuropharma Precision Olfactory Delivery (POD) claim improved targeting of key areas in the nasal cavity. A good device technology can make a big difference. However we shouldn’t forget that reading a well-prepared instruction for use (IFU) – and following it – can genuinely improve outcomes. Bad habits are readily learnt with OTC products as many of us simply throw the IFU away. Simple ideas can be effective; the ‘contralateral’ technique (left hand, right nostril and vice-versa) directs spray away from the septum and towards the turbinates.

A liquid dose above 100µl per nostril will generally result in wastage (down the throat, or onto the upper lip). Even at or below 100µl, the nasal cilia clear mucus rapidly and continuously so a slowly absorbed drug may be cleared (ending up in the stomach) before absorption, resulting in poor efficacy. Formulations which enhance absorption, or which encourage adhesion to the mucosa to allow controlled absorption (such as PecFent®; see above) have proved effective. Powder formulations, rather than liquids, are another response to the ‘100µl’ challenge, although mucociliary clearance still has to be dealt with. Preservative-free formulations have become increasingly common and are better for the patient in many ways, but multi-dose products do require device design changes in order to avoid contamination of device contents, given that these devices are regularly inserted into the nose.

### The device is the drug-to-patient interface, so it must be reliable and effective, but easy to use correctly.

To be therapeutically effective, the formulation must enable the active ingredient to be taken up by the target tissue. Get all this right and you can get excellent results – a piecemeal approach may be less than satisfactory.

### NOTHING’S EVER STRAIGHTFORWARD THOUGH...

And so it is with nasal drug delivery. Some problems have been encountered including:

**Damage to the nasal septum,** especially with frequent use of OTC decongestants. Without doubt, damage – ranging from crusting and soreness up to (very rare) instances of perforation – can arise. However IFUs generally stipulate that these products should not be used for longer than three to five days, whereas most instances of septum damage occur after extended periods of use. Quite apart from issues of septum injury, ‘rebound congestion’ – where the decongestant becomes ineffective with excessive use – means that ignoring IFU is pointless as well as potentially harmful.

An increased risk of cancer has been associated with the long-term use of nasal calcitonin in the treatment of osteoporosis. As a result, calcitonin nasal sprays were withdrawn from the European market in August 2012, in the US from March 2013 and Canada from October 2013. That said, it is worth adding that injected calcitonin also now carries warnings regarding long term use and increased cancer risk.

**In October 2000, a newly licensed nasal inactivated influenza vaccine was used in Switzerland, but 46 instances of Bell’s Palsy were reported amongst those treated.** Subsequent investigations indicated that this could have been associated with the specific adjuvant used yet the vaccine was withdrawn. Despite this, nasal vaccination continues to be widely accepted by regulatory authorities.

Just like any other drug or combination product, complications and issues may arise. So whilst every effort is made to identify problems prior to release, occasionally there are adverse reactions, sometimes leading to product withdrawal.

### WHAT NEXT?

Nasal delivery is not a universal panacea, but then neither is any other route of administration. Nasal delivery can do some things very well, however, and has some advantages including elimination of sharps, relative ease of use, and patient

acceptability. Nasal delivery has already been used to re-purpose several existing drugs and we can probably expect more ‘life cycle management’ applications of nasal delivery going forward. But if we look further toward the horizon, what then?

Delivery of biologic drugs to treat CNS conditions such as Parkinson’s, Alzheimer’s and stroke has been a mission for many years. Both OptiNose and Impel claim improved access to the olfactory region and in April 2013, Impel Neuropharma published results showing that their POD device was able to deposit a radiolabelled tripeptide into the deep nasal cavity with subsequent rapid and significant delivery to the CNS.

There is also interest in the possibility of delivering cell-based therapies to cure neurodegenerative disorders, such as Parkinson's disease. A very interesting study, led by the University Hospital of Tübingen in 2011, indicated that Mesenchymal stem cells, delivered to the brains of rats via the nasal olfactory region, resulted in substantial restoration of neurodegenerative damage and of motor function.

These are just a couple of examples and it is too early to suggest that a nasal spray can reverse the effects of a stroke or a similar human condition in the near term. But the progress made in the last 30 years deserves recognition. And in areas such as pain relief, emergency therapies, hormone delivery and vaccination, nasal delivery still has much to offer – providing we maintain a common focus upon the drug, the formulation, the delivery device and the patient.

#### ACKNOWLEDGEMENTS

Statistics for nasal delivery tend to get bundled with those for inhaled delivery, despite the fact that in general, the only common factor is association with the respiratory tract. As a result, it is difficult to extract specific figures for the nasal drug market. Team would therefore like to thank Dr René Bommer for his permission to use nasal drug market data researched and published by pharmAccel Consulting and also for his helpful advice and useful observations regarding the nasal drug delivery landscape.

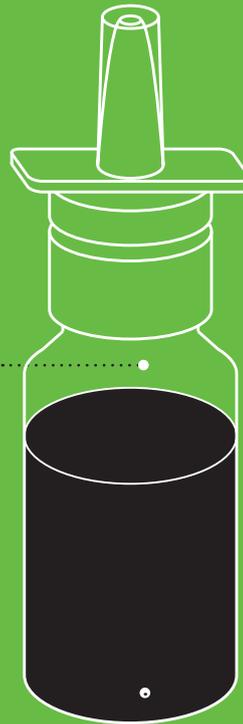


→ [andy.fry@team-consulting.com](mailto:andy.fry@team-consulting.com)  
*Andy Fry founded Team Consulting in 1986. He has been involved in development of nasal delivery devices since the early 1990s and is a named inventor on a number of patents.*

## NASAL MARKET BY VALUE

20 – 30 %

VACCINES  
HORMONES  
CNS  
BREAKTHROUGH CANCER PAIN  
RESCUE MEDICATION  
HEROIN OVERDOSE



\$8.5 BN  
ESTIMATED  
GLOBAL  
NASAL DRUG  
DELIVERY  
MARKET

70 – 80%

OTC DECONGESTANTS  
AND PRESCRIPTION  
ALLERGY THERAPIES

# THE USABILITY OF USABILITY

BY ROB FERNALL



→ [rob.fernall@team-consulting.com](mailto:rob.fernall@team-consulting.com)  
 Rob is a senior human factors consultant at Team and has over 20 years' experience across a variety of sectors.

usability	human factors	
ergonomics	user experience	information architecture
human factors engineering	usability engineering	user research
<b>goal</b>	<b>scenario</b>	<b>case</b>
<b>violation</b>	<b>rule</b>	<b>knowledge</b>
fore	use	user
essential	intended	mode
reasonable	nescient	based

step	error	task	action
failure	slip	lapse	mistake
non	un	ab	mis
usage	sub	critical	important
correct	anticipated	seeable	normal
attentional	omission	commission	violation

**There is a feeling in the industry that us human factors practitioners could do a bit more to make Usability more usable. I want to draw your attention to one important aspect: terminology. Now already some of you may be thinking “does he mean human factors or usability? Is there a difference? What is the difference?”.**

**So to illustrate the significance of the problem, here’s a little game for you using the tear-out cards on the left.**

## ONE

Tear out the twelve perforated terms in yellow and and put them into clusters of synonyms.

## TWO

Find someone who agrees with your clustering.

## THREE

Repeat steps 1 and 2 with the fourteen frequently used “use-error” words on the black cards.

## FOUR

Now tear out the remaining 25 white cards. This is where the fun really begins. Each of these cards has a word, or part of a word, which can be combined with other black cards or other yellow cards. As well as clustering, as before, you can now string cards together to construct existing HF terms such as “unforeseeable-non-critical-use-error”. You can also try to find the “popular” cards (ones can sit happily with a variety of other cards) and “loner” cards. You can create your own games and rules but we recommend you don’t generate new combination strings in case they start to become familiar-sounding phrases and inadvertently leak into everyday HF language.

## OBJECT

The object of the game is to appreciate the current sub-optimal situation with respect to HF terminology whilst remaining calm.

## FINAL THOUGHT

I shall dare to say (and feel free to shoot me down) that all the combinations of all the terms cover nothing more than the following...

Understanding when, how and why people go wrong when they use stuff; and whether it matters.”

Do we really need so many terms to cover that?

# The Usual Suspects

## Selecting materials for medical devices

BY CHRIS HURLSTONE

6'6"

6'0"

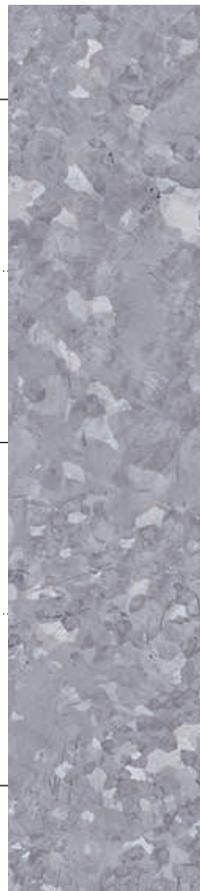
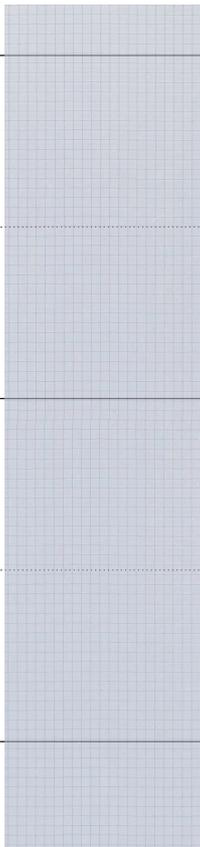
5'6"

5'0"

4'6"

4'0"

3'6"



When developing a medical device, selecting the right material for each part is a fundamental step, one which demands an understanding of issues ranging from physical performance and manufacturing constraints, to budget limitations and supply chain logistics. There are few 'trivial' components in a medical device and identifying materials for all but the most straightforward demands a robust decision process to ensure that appropriate options are assessed.

In medical device design, a number of key factors need to be considered when deciding whether or not a material, and its specific grade, is appropriate for use on a component:

### Mechanical properties:

Frequently the first characteristic to be considered when choosing a material as these determine its suitability for the functions that the component will have to carry out. Properties such as stiffness, toughness and yield strength quickly narrow down the options, while additional factors such as environmental conditions of storage and use (hot, cold, humid and so on), and loading conditions (compression/tension, continuous/cycled, single or repeat use) will help the engineer home in on potential candidates

### Surface properties:

Hugely important when assessing possible materials, particularly if friction plays a crucial role in successful device operation. If friction co-efficient data is unavailable for the material combinations under consideration (which is often the case), then further analyses and testing is frequently required to check performance of the specific grade combinations chosen. Surface properties can also significantly influence scope for processes such as bonding, labelling and printing.

### Physical properties:

Broader physical properties such as density, transparency and electrical conductivity are critical to many applications, including some not immediately evident (for example, a build-up of static electricity on a component in the drug path can significantly affect the performance of a dry powder inhaler). Physical properties can also impact on manufacturing options such as injection moulding processing or, for assembly, ultrasonic or laser welding.

### Chemical properties:

These can influence resistance to degradation through contact with lubricants, solvents, moisture or electro-magnetic radiation (such as UV light), and can also raise concerns about susceptibility to the influence of sterilisation techniques such as gamma or ETO. The chemical make-up of a material also determines whether certain moulding techniques such as co-moulding can be used to achieve, say, a multi-textured exterior finish (for 'soft-touch' grips) or different features within a single part (a clear window within an opaque body or casing, or a compliant sealing element for example).

### Rheological properties:

Relating more to manufacturing considerations than performance in use, properties such as melt temperature and viscosity have a major impact on injection moulding capability, and hence can rule out some materials for components with sections that would be difficult to fill. They can also influence a material's tendency to 'sink' or 'flash'.

Shrinkage rates can also affect component stability, especially if rates are different parallel and perpendicular to the flow, and hence they potentially limit scope for the designer with respect to part geometry. Component design influences material selection and vice versa; the decision process is not 'one-way'.

### Biocompatibility & stability:

Key requirements for many medical devices, especially drug delivery devices which must be made of materials suitable for contact with both the drug (that they do not influence drug characteristics, and are not influenced by them) and the user (such as skin contact or implantation – long or short term). For materials not already approved, extensive test programmes could be required to check extractables and leachables, toxicity or irritation, depending on the application and risk. For considerations such as long term implantation or drug primary packaging, where permeability to substances including moisture or oxygen can also be key properties, these issues can be the dominant factor driving material/material grade selection.

### Colour:

An important element of product design and often used to help create the visual language necessary to encourage correct use, and to make a device more 'appealing'. But colour selection for medical devices can present a number of different hurdles. Only a limited palette is approved as medical grade, for example, constraining choice for device designs unless budgets and timescales can accommodate a lengthy approvals process. Colour – or colour change – can also impact on moulding tolerances, highly relevant when components feature tightly controlled critical dimensions.

### Feel:

Materials contribute significantly towards the physical feel of a device, giving the user important tactile and visual clues. An expensive device has to look and feel solid and substantial, whereas a disposable device may need to be considered 'OK' to be thrown away guilt-free. Any requirements for audible feedback, such as device 'clicks' to indicate correct use throughout the lifetime of the product, will also have a bearing on material selection.

## Cost:

Almost always a factor in the decision making process, and for devices in highly competitive markets this can be the dominant driver. Materials selection can become a process of 'moving up the price list' from materials and grades which are 'affordable' but which aren't quite up to the job to ones which challenge target product costs but which can deliver technical performance. This is not an ideal approach; selection should be based, wherever possible, on technical criteria, but devices need to be commercially viable as well as technically sound, and compromise is often required, where risk profiles permit.

In an ideal world, all of these different factors would be considered in an organised, structured fashion as part of the design development process, resulting in a clear set of component materials specifications for the device. In reality, however, material selection rarely occurs as a steady progression through a strictly defined decision tree. It is invariably influenced by other factors – borne out of the reality of the development process – which makes a theoretically well-defined process less straightforward than might be expected.

To begin with, material selection demands discussion between a number of different parties, all of whom bring different and influential perspectives to the negotiations. These are likely to include:

### Device developers:

Continually seeking the best combination of industrial design and mechanical engineering, driven by the 'vision' for the device and by user needs and aspirations, branding and visual language, and the need for reliable and robustly performing devices produced from capable manufacturing and assembly processes. All at the target cost. Within the development team itself there may be different and sometimes conflicting views on the best way to achieve good solutions, and there can be many potential compromises with no clear favourite. It is imperative that the device development team understands the different priorities and perspectives at work and is also not too influenced by personal material preferences. There can be a strong tendency to 'trust' a material used successfully in the past, even if the new application is slightly different.

### Materials suppliers:

Key partners in materials selection, able to provide detailed information and recommendations on the materials and grades they supply. They are, of course, primarily focused on their own product range and hence not necessarily best placed to give broad, independent

advice. Building good relationships with a range of materials suppliers, including some independent organisations, is one way to help ensure that balanced views and recommendations are obtained. It is also often the case that detailed information required for some engineering analysis such as FEA, Mouldflow and fatigue or creep calculations may not be available from the suppliers for the grade under consideration. If there is neither the time, budget or resources to generate this data - and engineers should not be surprised to be told that the amount of material for an application is too low to warrant such investment - a designer may be pushed to make assumptions, which can be risky, or chose a grade for which good data is available, which may result in compromise.

### Component manufacturers:

The people who, at the end of the day, will have to manufacture the device, in the quantities required, in a commercially viable way - which means low reject rates, straightforward inspection, low tool maintenance and so on. They may be limited to - or prefer to stick with - existing technologies, processes and supply chains and hence may not be open to new material options. They might also have preferences for certain materials with, for example, wide processing windows or well understood storage and handling procedures.

### Registered device manufacturers:

Responsible for placing the device on the market, and focussed on the need to ensure that it will be safe, commercially viable, will meet regulatory requirements and can be manufactured reliably in the volumes and geographical locations required. Risk reduction is a key driver, so they may prefer well established 'industry standard' materials compared to newer or less frequently used polymers and grades, especially those where the supply chain is less well established.

**material  
selection  
rarely  
occurs as  
a steady  
progression  
through  
a strictly  
defined  
decision  
tree**

## Unexpected events and late design changes

As well as the influence of individuals, 'events' can also complicate the matter of material selection. Health scares – justified or unfounded – can very quickly shift industry or regulatory opinion and render some materials suddenly unacceptable, or at least highly restricted. Examples include the risks centred on formaldehyde release from acetal polymers which became a serious issue in the 1990s, or recent concerns over potentially carcinogenic Bisphenol A residues in polycarbonate containers. For this or other reasons, some suppliers may suddenly decide to withdraw approval for the use of their material in medical applications, especially if higher production volumes are coming from sectors other than healthcare, and the added control and documentation overheads required by medical device supply may simply not be worthwhile.

With environmental concerns rising up priority lists for many companies, the desire to use recyclable materials – or at least materials offering minimal environmental impact on disposal – is increasing, which introduces a new selection criteria for consideration.

And finally, back to the bottom line. Changes in raw materials costs, such as oil prices, can significantly affect price – and availability – of a desired polymer or grade, adding further uncertainty to the economic aspects of material selection.

Once a preferred material is selected and designs detailed, it will be hoped that no further changes are required. However, updates to device requirements late in the day, or changes in the understanding of a design envelope – for example when issues are discovered during performance testing – are just two instances that may prompt a material change late in a development programme, which can be extremely time consuming and expensive to implement.

Some design changes result from issues with 'bulk' properties of the material, such as the creep performance of a plastic spring element or the stiffness of a retention clip, but these issues should

have been identified and resolved earlier in development. Performance issues late in the day are frequently associated with surface properties, such as: excessive friction leading to poor mechanism function; poor stability with a drug due to surface interactions; reduction in impact strength due to micro-cracks, discovered during drop testing perhaps; degradation in properties due to surface contact with other substances; labelling/bonding/printing issues due to low surface energy. German physicist Wolfgang Pauli (1900-1958) summed it up nicely when he said: "God made the bulk; surfaces were invented by the devil".

All of which may seem like an endless set of hurdles to overcome, but it's not that bad. To begin with, surfaces can be modified... With thorough forward planning, rigorous empirical and analytical development work, good relationships between all stakeholders involved, and detailed consideration given to materials selection from early on in the design process, it should be possible to identify the ideal materials for a medical device. With almost 4,500 materials and grades of plastic and elastomers on the Campus database for a start, there are quite a few to work with.

# God made the bulk; surfaces were invented by the devil.



→ [chris.hurlstone@team-consulting.com](mailto:chris.hurlstone@team-consulting.com)  
Chris is director of engineering and has a strong track record in delivering innovative solutions to many of Team's international clients.

# MULTIPLE PERSONALITIES

Every experienced project manager knows that it's not the methodologies that are key to a successful project, it's the softer people skills. The careful management of individuals such as technical specialists, project sponsors, suppliers and strategic stakeholders, and the ability to bring them together to form a coherent project team.

When you are working at the leading edge of medical product development you inevitably come across challenges. Sometimes these potential challenges are identified early in the project and you prepare for them accordingly, other times something changes that you have no control over and these really test your resolve.

This got me thinking. What makes certain people good at project management? What is it about their skill set and personality that makes it just work? Keeping calm is important at times, but so is the ability to adapt and inspire. Being fair, a good listener, making difficult decisions and then leading the team to a successful conclusion. A good project manager needs multiple personalities!

BY SOPHIE RAVEN



## BANK MANAGER

We have to keep a finger on the financial pulse, balancing committed cost with anticipated future spend, understanding each stakeholder's commercial desires, and managing the expectations of all team members accordingly. While this is often about managing clients' expectations, the bigger challenge is always to focus the minds of the technical team, allowing them to push the boundaries without blowing the budget!



## MEDIATOR

When working with a broad range of personalities, from marketing professionals to manufacturing and production engineers, differences in opinion are inevitable. Whether within the core team or at a higher strategic level, this requires finely tuned mediation, negotiation and conflict resolution skills.



## COACH

The key to any successful project is a motivated project team. This is about understanding people as individuals, their strengths and drivers; then it's about formulating a plan to utilise these individuals' best abilities, perhaps substituting resources as the project develops and different skills are required, but always ensuring that the team is pulling together and working towards the same end goal.



## PSYCHIC

Predicting the future... or at least having a sense when something doesn't feel right, is a vital skill. This is partly risk management and partly gut feel, but it's also about having the experience and foresight to either avoid potential issues in advance or have a plan B in place to call upon if required.



## LEADER

Motivation and vision are a given, but we need to combine this with charisma and enviable communication skills, always welcoming and with the ability to adapt style and vocabulary to suit specific scenarios, cultures, technical background and levels of seniority.



## POLICE OFFICER

We have to know the 'rules' that must be adhered to, and we must enforce them. We must maintain a working knowledge of relevant standards and regulatory requirements, while being conscious of the risk of infringing existing intellectual property, and tackling or mitigating any potential projected-related issues before they escalate.



## YOGA TEACHER

You need to be calm and composed at all times, especially as things never go according to plan, and there is always a need for flexibility and creativity in dealing with challenges. This could be a change in scope or project direction involving anything from timescales and budget to drug formulation or user's needs.



## DETECTIVE

To really get to the root of any problem we must understand enough about the technical aspects to challenge the design, while keeping in mind what will make this product a commercial success, and then being able to pull the team together to converge on the right answer.



## RUNNER

whether it's a fast turnaround sprint of a project, to solve a pressing problem, or a longer running full device development programme, setting and maintaining the right pace is key. There will be pain barriers along the way and leading a team through them will require huge amounts of determination and drive.



## AERIAL PHOTOGRAPHER

When everyone else is absorbed in the detail, we must be able to stand back and see the big picture. We need a clear vision of the end goal, and an understanding of the market and (ultimately) the client's needs, while remaining focused on the project in hand.



## WISE MAN

Being able to lead the team through periods of change or uncertainty, whether in project scope, recourse or just progressing to the next stage of the development, can often be an uncomfortable process. Managing this uncertainty takes sensitivity, composure and calm. When in need of help or advice you are the 'go to' person, offering support and guiding the way to resolution. You need an air of authority to ensure peace and harmony are maintained.



→ [sophie.raven@team-consulting.com](mailto:sophie.raven@team-consulting.com)  
*Sophie joined Team in 1998 as an industrial designer. She has built up a vast amount of experience across a diverse range of projects, ranging from drug delivery devices to QC test equipment.*

# Let's make things better

We are recognised globally as experts in the design and development of medical devices. That's all we do and we are proud of this focus. It enables us to deliver real insight and expertise to our clients.

Commercially successful products need to be safe, easy to use and ultimately make people better. Our clients like our approach, which combines design, human factors, science and engineering from inspiration right through to industrialisation.

Everybody at Team is driven by the same desire, to make things better by working in collaboration with clients and each other. Whether 'things' means people or the products we work on, we apply the same commitment to do the best and be the best that we can.

This focus and desire is a powerful combination and one that highlights why our clients trust us over and over again.

Team Consulting Ltd.  
Abbey Barns,  
Duxford Road,  
Ickleton,  
Cambridge  
CB10 1SX, UK

+44 (0)1799 532 700

[info@team-consulting.com](mailto:info@team-consulting.com)

[twitter.com/team\\_medical](https://twitter.com/team_medical)

[slideshare.net/team\\_medical](https://slideshare.net/team_medical)