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Advances in medicinal chemistry evaporators: an interview with Alison Wake, Genevac

Published on March 8, 2016 at 7:44 AM

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insights from industry

Alison Wake

Product and Marketing Manager,
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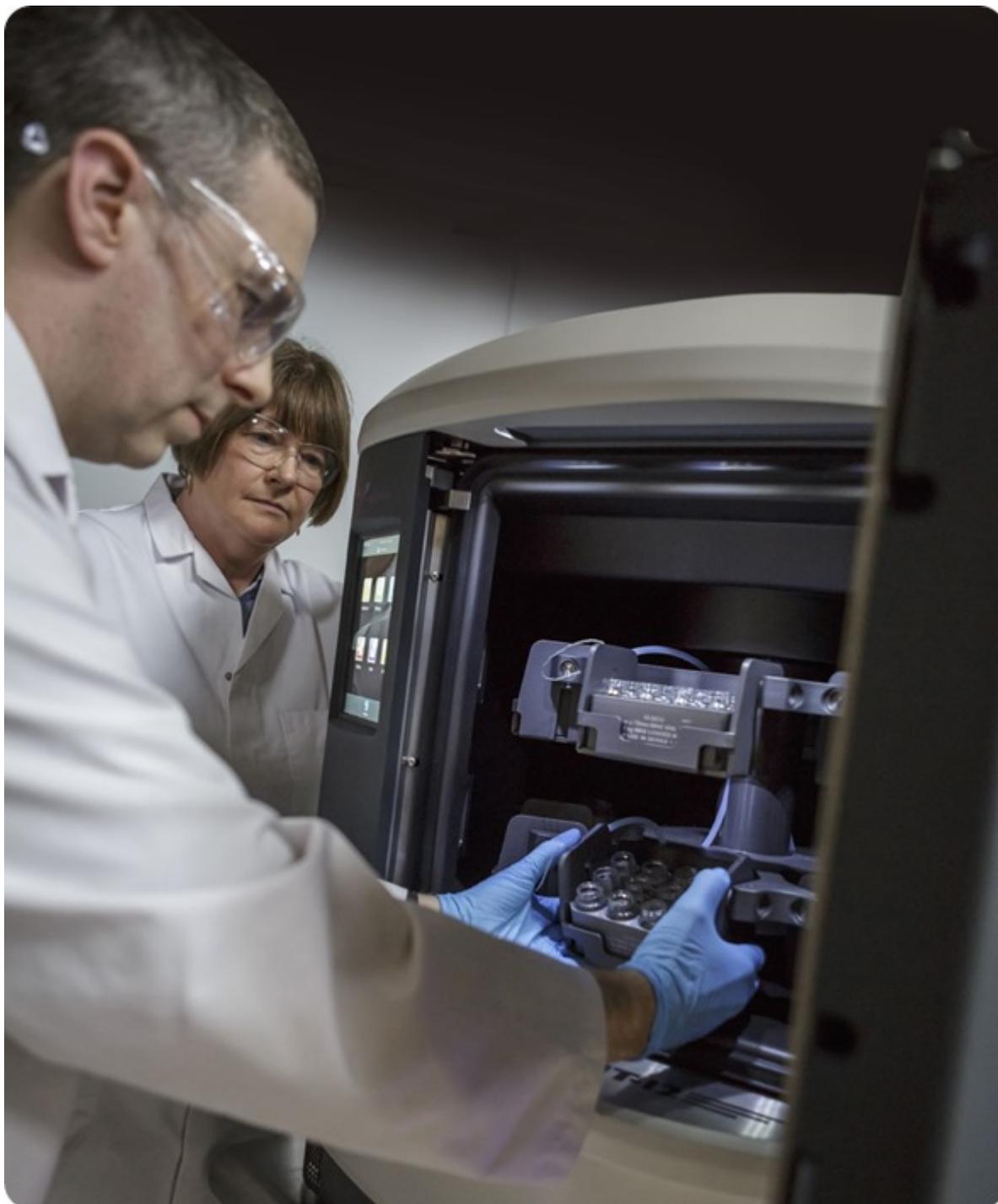


Interview conducted by April Cashin-Garbutt, MA (Cantab)

How have High Throughput (HT) evaporator systems advanced since the 1990s?

The Genevac Series 1 System, which was launched in the mid 1990s, had no programming as such. It was a very basic system – it had basic vacuum control and a timer of sorts. It was very similar to the current myVac evaporator system we use for molecular biology and biological applications.

The Series 2, which was released around the turn of the millennium, has had ongoing development during the last 15 years. We introduced scroll pumps to give more reliable vacuum, better and lower temperature condensers and high power lamps. There were advances in programming for applications such as lyophilization and eXalt crystallization. We've also introduced SampleGenie, which is a way of concentrating directly into a vial from larger volumes.



Genevac's Series 3 HT Evaporator Brochure

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The Series 3 HT evaporator consolidates all the improvements that were made with the Series 2, but it also has an improved design, a much better user interface, improved sample guard temperature monitoring and better ergonomics. The applications are better, and are going to be even better, because of an easier programming system and an in-built capacity for further advances in applications going forwards.

What are the main challenges when high numbers of samples require evaporation in parallel?

Medicinal chemists often use rotavaps, but those will only evaporate one sample at a time. When you have high numbers of samples, evaporating sequentially isn't practical, you need to be able to put all of them into the same system.

With that, comes the risk of cross-contamination, which is probably the most significant risk. Genevac has addressed this with the Dri-Pure system, which controls the vacuum and the rotor speed to prevent bumping and cross-contamination, particularly in solvent mixtures. Certain solvents are more prone to bumping and therefore cross-contamination and we've got papers that prove that our systems remove the risk of cross-contamination from bumping.

Another issue is the detection of dryness. You don't want to keep evaporating your samples once they've actually become dry. For that, you also need good temperature control. Our Sample Guard system of probes, which monitor the temperature of the holders, can also monitor the temperature of the actual samples and detect sample dryness. Also, the system automatically stops when the samples are dry. That in-built protection means you don't overdry and damage your samples.

Achieving even drying with multiple samples is another issue and our sample holders are specifically designed to give even temperature control; they're made of aluminium and they're designed so that all the samples get the same amount of heat energy.

Another factor is the large solvent volumes that can be involved if you've got a large number of samples. Every condenser has a limited capacity and Genevac have introduced autodrain and defrost functions so that the system can automatically drain the condenser mid-run and allow for higher capacities.

That also helps with the solvent mixtures you often get. For example, if you're drying down fractions, you've got mixtures of water and acetonitrile in different combinations and having the autodrain and defrost means you can have multi-stage programming to take off the volatile and then change the parameters to take off the less volatile water elements.

How have recent advances in condenser technology impacted lyophilisation?

Genevac developed Fast Lyo. It's fast evaporation, where you concentrate the samples down until you've got about 1 to 2 mls of sample left. Then, you can actually lyophilize that rather than lyophilizing 10 mls, that can take a long time to freeze dry. Essentially, you can condense and then lyophilize a small amount.

The lower temperature of our most recent condensers, together with the automatic draining mid-run, has helped develop this and make it more efficient. It also gives a better evaporation of mixtures. A volatile solvent is collected in the condenser at a certain pressure. Then you make the pressure lower to either lyophilize or take off water, but you can actually get the solvent boiling off from the condenser. However, with an auto draining condenser, or a condenser that's got a very low temperature, the solvent stays in the condenser and doesn't spoil the vacuum.

This also means you can have improved lyophilization because you can trap your organics and still have some organic solvent around in the sample when you're actually lyophilizing. At a lower temperature, you can still trap the low boiling point organic while you're pulling very low vacuum to achieve lyophilization.

Can you please outline Genevac's Series 3 HT evaporator system?

Genevac's Series 3 HT Evaporators

[Click here formore information](#)

The Series 3 HT is the latest design of the renowned Genevac HT (high throughput) evaporation system; The Series 2 HT became the evaporator of choice for medicinal chemists worldwide. It's a centrifugal vacuum evaporator capable of evaporating large numbers of individual samples all at the same time, both safely and quickly.

It's the only evaporator in its class that is capable of meeting the demands of medicinal chemists nowadays, such as very high numbers of samples, high boiling point solvents, mixtures of solvents, HCL and fast lyophilization.

Series 3 retains all the features and functionality of the Series 2, but it has updated and additional features and is much easier to use.

What customer feedback was taken into account when designing the Series 3 HT?

One of the main things that people said about the Series 2 was that the user interface was difficult to use. The Series 2 was seen as being clunky and complicated and they often didn't get the best use out of the system because they found it difficult to program. They wanted something that was going to be easy to use like the EZ-2 that we have, where you just program in a solvent type and it does it all for you, but they also like the programmability of the HT, in that they can program it specifically for the evaporation parameters they want.

The other problem was that the systems could be difficult to load. The HT-12 had three layers of rotors stacked on top each other. The top rotor could be quite difficult for small people to load. The HT-4 would top load, so again, you would have to get up and load it as you would a centrifuge, which could be difficult.

With the Series 3, we created a six place rotor and made both versions of it, the HT-6 and HT-12, front loading. There are only two layers with the 12 place. With both, you front load and you don't have to reach across the top like you do with the HT-4.



Also, bench space and fume hood space is at a premium, so the less that we could take up of that, the better. We therefore made an integrated condenser. There's no separate condenser and it's all contained in one footprint. They also wanted user changeable lamps because, traditionally, changing the lamps involved a service visit. The user

changeable lamps was something that just made things easier to use and meant less down time.

They also said that the Series 2 was a bit dated and old fashioned looking. They asked for a new look, which we have given it and it's beautiful now!

What are the main benefits of the Series 3 and what feedback have you received so far from users?

The main benefit is the ease of programming. The users didn't get the best out of the Series 2 and the new user interface is very easy to use for both experienced and inexperienced users. It gives experienced users the ability to tailor their methods much more easily than they did before.

Programming the system is easier which has meant improved efficiency for customers and better use of their time. More users can actually use the system and use it to its best potential because it's easier to use.

The smaller footprint allows better use of bench space and fume hood space and the front loading is easier. Also, you can get in from the front. It's easier to clean and there are lights inside so you can actually see what's going on in there, which makes it much more user-friendly.

In summary, the feedback from customers is that it's much more user friendly than the old one, it offers better efficiency, and the extra bench space is welcome. It offers all of these benefits, while still having the same capabilities and more.



Please can you give some examples of successful applications of Genevac's Series 3 HT?

The Series 3 can obviously be used for all the same applications that the Series 2 could be. The main applications for that have been in medicinal chemistry and drug discovery in general, in synthesis and purification.

The easier operation of the Series 3 means it's possible to operate and expand into other applications where people, traditionally, maybe haven't been aware of Genevac and haven't used the Genevac high throughput evaporation system, such as for natural products, food and flavors research and fuels research. This system is easier to use and people are more open to using a new system if it is easier to use.

We have got a particular customer who's using the system in conjunction with their prep chromatography system, a Sepiatec Sepbox, which generates an extremely high number of samples. I think it can produce just short of 600 fractions in one run. The HT or paired HT systems alongside each other can easily dry all these fractions in one go.

Can multiple Series 3 systems be installed side by side?

Yes. We have a specific Infinity Trolley, which is designed to accommodate the system with the pump and the waste solvent underneath on the lower shelf.

The infinity trolley also means you can move the system around quite easily. It's got a lower platform that moves out to stabilize the system because it's obviously quite a heavy system, but you can put it on an infinite trolley and then move it around if you want.

They can actually be put quite closely against each other, into a large fume hood. We used to produce the HT-24, which was like an integrated, two 12's on a trolley, but now you can effectively have an HT-12, HT-24, Ht-36 or whatever you need, basically.



What changes do you plan to make to the HT system moving forwards?

We've developed a programming wizard on the system, which is an onboard automatic programming based on the solvents that are being evaporated, their relative volumes and the sample format (e.g. tubes, flasks or micro-

plates).

We've used the knowledge that we've gleaned from producing programs specific for different solvent mixtures and incorporated that into this automatic wizard. We'll be looking to expand that with further solvent mixtures and other solvents, so that's an ongoing project at the moment.

There is the possibility of putting a high specification pump on there to give better performance with the high boiling point solvents and possibly to accommodate some higher boiling point solvents.

We're also reviewing our sample holders because with the new rotor design, it's possible to accommodate either more sample tubes in there or longer sample tubes, so we've got the opportunity to have a higher capacity across the range.

In addition, of course, we'll respond to any customer requests regarding what people would like us to develop and add to the system as they start using it.

What do you think the future holds for evaporators used in medicinal chemistry?

In recent years, medicinal chemistry has moved away from the old traditional combinatorial chemistry methodology, which produced many hundreds of compounds and as many compounds as possible, to a more focused approach with less compounds actually been worked on in each project. High throughput systems will always be required in medicinal chemistry but there will also be a requirement for increased flexibility.

For example, we've got our Rocket System, which is capable of handling six 450 ml flasks. It can also do a 5 liter batch and has a feed system. That and the high throughput systems give you range in that you are able to handle many hundreds of very small samples, right up to a hundred liters of sample and drying it. Therefore, I think that flexibility is going to be key.

Also, there is the general ease of use that we're developing and the time saving that offers, not just with regard to the speed of the operation, but the time saving for the actual operators. You can walk away from our systems; you don't have to monitor them, which frees up time for scientists to go off and do something a little bit more interesting than watching rotavap.

Where can readers find more information?

More information can be found on our [website](#)

For any questions, please email salesinfo@genevac.co.uk

About Alison Wake

As [Genevac](#) Product and Marketing Manager I am responsible for product development and global marketing of the Genevac range.

Originally from a medical laboratory background, with an MSc in Applied Science from Sheffield University UK, I moved from the lab into the commercial sector in 1999.

I worked in several biotechnology and laboratory equipment supply companies, in both Scientific and Sales roles, before joining Genevac 10 years ago where positions have included Sales Consultant and Distribution Manager.

Genevac is a global leader in centrifugal evaporation systems and is part of SP Scientific, a leading manufacturer of specialty equipment for pharmaceutical, biotechnology and industry.



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Company Background

Genevac's high performance centrifugal solvent evaporator systems are designed for use in chemistry, biology and analytical science applications and are in use in laboratories worldwide.