Interview

Maximizing
the Value of Biospecimens to Deliver *New Therapies*

with Clive Green, PhD, Director and Head of Sample Management at AstraZeneca

Introduction and Background

This eBook originated in a presentation by Dr. Green, entitled “Business Planning to Deliver Value for Pharma,” delivered at the 2015 Annual Meeting of the International Society of Biological and Environmental Repositories (ISBER).

In his position as Director and Head of Sample Management, Dr. Green is faced with a number of challenges, including AstraZeneca’s transition from their research and development center in northwestern England, to a new research center to be built in Cambridge. The greater challenge going forward is, from Dr. Greens’ perspective, maximizing value from the biospecimens in the collection. This involves, among other issues, closing the gap in inventory management methods between the small molecule world and the world of biospecimens. In this interview, he shares his perspective on biobanking, as it compares to managing a small molecule inventory, and challenges in the biospecimen supply chain.

CLIVE GREEN

Clive Green, PhD, is responsible for the small molecule sample collection and the UK human biological sample biobank that supports AstraZeneca’s Innovative Medicines and Early Development (IMED) Biotech Unit. The mission of the IMED Biotech Unit is to discover potential drugs and develop them to the end of Phase II clinical trials. Dr. Green has 10 years of experience in medicinal chemistry and drug discovery, focusing on oncology and cardiovascular disease areas. He has served as an Associate Director in medicinal chemistry, and his research activities have spanned all phases of drug discovery research. He became Head of Compound Management in 2010, and assumed responsibility for AstraZeneca’s human biological samples, in addition to the company’s small molecule collection, in 2014.

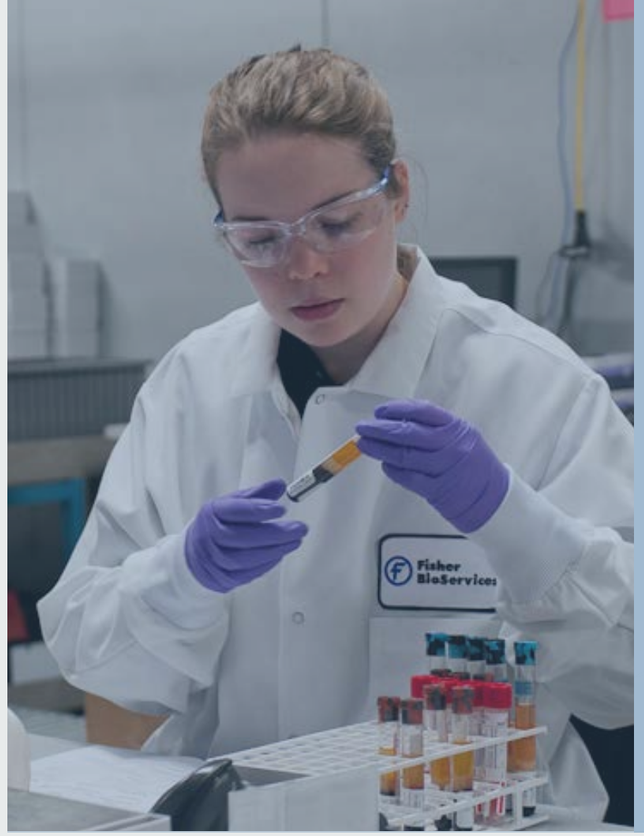
Dr. Green earned his PhD in Organic Chemistry at the University of Nottingham, and also spent two years as a Postdoctoral Research Fellow at the University of Pennsylvania. He has co-authored numerous research articles and abstracts in medicinal and analytical chemistry, pharmaceutical chemistry, and related topics.

Share this ebook!

01

Q:

Thanks, Dr. Green, for speaking with us today. Your presentation at ISBER included a discussion of how biospecimens drive value, and about logistics and rapid access to specimens. Can you elaborate on this?



A:

Rapid access to samples is essential in understanding human target validation earlier in research and optimizing the clinical trial process. Consequently, increasing the speed of operations is a primary focus among my colleagues both from clinical disciplines and biobanking, and this means just-in-time processing of samples by the biobank. Speeding up drug development means responding faster to what is happening in the clinic and getting samples to researchers far quicker than we have in the past.

There is a mindset that it takes many years to develop a new therapy. But companies are challenging this mindset—aiming to ensure the development process does not consume more time than is necessary, in order to deliver new medicines to patients faster. We need to be faster in the clinic and more agile with the samples. We believe that it should take no longer than 48 hours from a researcher requesting a sample to having the order processed and dispatched to them. In the small molecule arena, which we also manage, our service level agreements are to process more than 95 percent of all requests within 24 hours.

02

Q:

Can you talk more on the differences between supporting small molecule research versus biospecimen-based research?

A:

There are many similarities—receiving, laboratory processes, storage, retrieval and reformatting, global logistics—there is a lot of overlap and many of the same challenges. But there are also differences: small molecule research compounds have no intrinsic link to a patient. They originate in internal chemistry campaigns or commercial acquisitions, so the methods for controlling use are amenable to simple IT applications. With biospecimens, consent can differ between clinical studies, and ethical perspectives can be translated into different legislation across territories, which also continually evolve. And sample quality is not easily or routinely measured throughout the sample lifetime.

The utilization rate between the two sample types also offers an insight into the difference. For instance, AstraZeneca added about 210,000 biospecimens to inventory in 2014, with about 60,000 shipped out of the collection for use in research. In the same year, the company added about 45,000 compounds to the small molecule inventory, with 1.15 million used for research. Whilst we should expect to see a difference in the utilization rate due to the very different roles the sample types play in research, the experience from small molecule research helps us to understand that greater utilization of biospecimens should be possible. Colleagues in biobanking have discussed achieving a 1:1 utilization rate–the same numbers of samples being added to an inventory as those being requested. This is a realistic medium-term goal that will provide greater value through scientific research.

Share this ebook!

03

Q:

What are the primary issues with regard to getting the most value from a biospecimen collection?

A:

Historically, samples were collected and consented for a specific purpose defined in the clinical study protocol. Increasingly, scientists have recognized that human biological samples are valuable research tools for the discovery of new medicines, and have sought to obtain broader consent for future use of samples in research. This led to the practice of banking specimens and then annotating them with data that could support future utilization. Going forward, we aspire to annotate the samples before we bank them, so we know whether or not the specimen has value in exploratory research, beyond the intended use of the sample in the clinical trial. We can't know precisely what we will need, of course, but we should rely on the judgment of our clinicians and researchers to determine what to bank.

The other primary issue, from my perspective, is the biospecimen supply chain supporting exploratory research. Compared to the small molecule world, we have a long way to go. There is a gap between what constitutes excellence and what is actually being delivered, and that gap needs to close quickly. The amount of time it takes—five to 10 days—to process samples for researchers must be reduced and the operations simplified.

The service level agreements in biospecimen management have reflected the pace of clinical activities. However, if we are to deliver new therapies to patients faster, biospecimen management has to adapt to new research timeframes.

We should work toward service levels of 24 hours, reflecting what is routinely achieved in small molecule compound management. Addressing the significant challenges and complexities that stand in our way will require investment in automated processes and IT, but equally important is collaboration across the scientific and operational disciplines, with a focus on driving projects to deliver new medicines. This is where the small molecule world was 20 years ago—local, manual storage in non-standard, un-barcoded vessels, with no transparency to inventory, quality and usage criteria. But now, small molecule sample management is a very disciplined and efficient process—standardized lab ware, fully automated processes with advanced technologies for reformatting and quality control, and broad use of samples across projects and with partners.

Share this article

Q:

In your ISBER presentation you talked about disrupting the old operational model. How has the shift towards personalized medicine impacted the flow of biobanking elements in this old model?

A:

Our previous model for biobanking capacity was based on retrospective data extrapolated over the next three and five years. However, with expansion of our clinical development portfolio and the application of personalized healthcare strategies (selecting appropriate and optimal therapies based on the needs of the individual patient) we now predict significant growth in sample collection due to increased patient populations and support for diagnostic testing.

This potential increase led us to prioritize our capabilities, thoroughly understand our costs,
and seek opportunities for closer collaboration with colleagues to work differently whilst improving support to our projects. As a research biobank, our focus is firmly on biospecimens in active use by our projects for research, and this set the design scope for storage and processing of biosamples at our new facility in Cambridge.

This is where collaboration with external partners is critical to our success: Fisher BioServices provided flexibility in storage space for archive biosamples, so we didn't need additional biobanking capacity at our new facility.

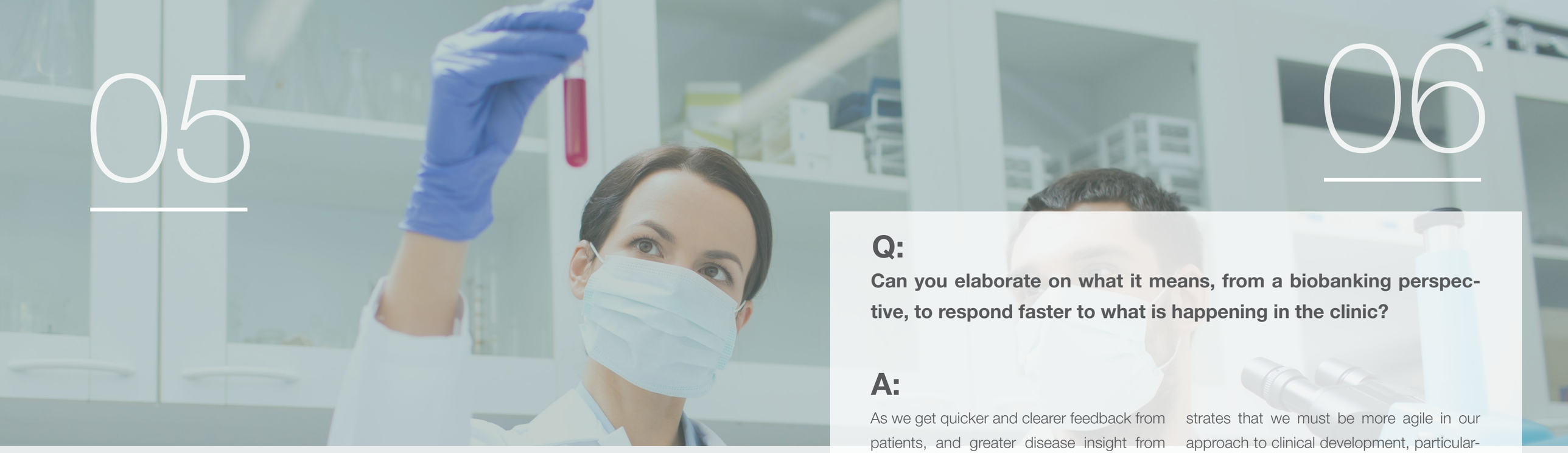
A significant externalization activity will generally lead you to re-evaluate business processes, and externalizing archive sample storage provided an opportunity to further improve our inventory management. However, some of the features of small molecule inventory management, such as individual vial retrieval, is more challenging in the ultra low temperature environments used for biospecimens and will require investment in innovative technology and standardization.

For now, we are putting controls in place so we don't re-introduce variability or reduce efficiency. We are ensuring that appropriate consent for future research is in place, that we don't retain more samples than we need, that our processes are standardized, and that critical information flows with the samples. Our success is dependent on increased collaboration between our research and clinical divisions, and with our external partners; close cooperation is pivotal in providing an environment for our projects to respond rapidly to the latest scientific information.

Externalization of the Archived Samples

In planning for the move to Cambridge, Dr. Green's strategy was to split the collection into two parts. Those samples currently in active use (about 52 percent) for research programs would be retained in-house, while the archived samples (about 48 percent) would be stored at a repository partner facility, Fisher BioServices. Although the samples to be externalized were archive samples, having them readily available was still a priority; Fisher BioServices' UK facility is located in Bishops Stortford, about a 40 minute drive from Cambridge. By archiving samples at Fisher BioServices, total annual costs were reduced and the space needed for biobanking at the Cambridge facility dropped from nearly 300 m^2 (about 3,200 ft^2) to only 135 m^2 (1,450 ft^2).

Share this ebook!



05

Q:

How do external partnerships enable AstraZeneca to focus on core capabilities?

A:

Where activities are important, but not urgent, opportunities may exist to work with external partners and leverage benefits through their core competencies and economies of scale. And of course, quality is a key consideration, but we can't assume that quality will always be higher by retaining activities internally. I think that if you partner with people who have credibility in the industry, a passion for their core business and a willingness to innovate, they can offer high quality services that complement the scientific innovation we deliver internally. One of the challenges in externalization partnerships is ensuring an appropriate degree of innovation so that opportunities can be generated and implemented to improve future quality and value.

06

Q:

Can you elaborate on what it means, from a biobanking perspective, to respond faster to what is happening in the clinic?

A:

As we get quicker and clearer feedback from patients, and greater disease insight from diagnostic tools and biomarkers, we learn more about the diseases we're targeting and how they progress. This generates opportunities for additional translational research in the midst of clinical trials, which require clinical samples for additional assays. Transparency to the status and availability of samples is of paramount importance, since the additional scientific information generated from translational research experiments can play a significant role in shaping the course of clinical studies.

This serves to underpin the obvious importance of human samples in developing medicines and treating patients, but in striving to deliver new medicines faster, it also demonstrates that we must be more agile in our approach to clinical development, particularly in ensuring we can provide appropriately consented biospecimens for exploratory research.

Several options exist to speed up the flow of samples for exploratory research—broad consent for research, new sample tracking IT tools, and immediate banking of samples for research. Given the current complexity of physical sample and information flow, solutions that simplify these processes are likely to be the most effective and have a greater impact.

Share this ebook!

07

Q:

Can you tell us more about transparency in the supply chain and just-in-time use of samples?

A:

All the samples collected within a clinical study plan must be available for analysis to determine if the study has met its end points. The challenge is ensuring that the samples, and their status, remain visible to other researchers. In some instances, for example, where patient populations are small, certain sample types could be very scarce. In circumstances where these samples have appropriate consent and are needed for translational research, we need processes that channel them to researchers in the shortest possible time after completion of the clinical study.

08

Q:

What is the current process in developing a biospecimens collection? How are you working to get more value out of such collections?

A:

The majority of our biospecimen collection originates from our clinical trials. We also acquire samples from commercial vendors and through collaborations with institutional partners. When samples have fulfilled their primary use and have appropriate consent for research, we strive to access the true value from them by ensuring their utilization in the discovery of new medicines. Consequently, we have to consider the questions, “what is it that researchers are looking for when they search an archive inventory of biological samples? What data makes them valuable for research?” For instance, we know that consent, gene mutation analysis, diagnosis and treatment history, and sample QC are critical to the value of samples. If this critical data is missing, then we are storing samples that are highly unlikely to be requested.

We can consider three different approaches to collecting the associated data—upfront investment in sample annotation before the sample is banked, investing in annotating some or all of the samples placed in storage, or waiting until a researcher identifies a sample that could be important. Whichever approach we take, by addressing the challenges of sample annotation, including appropriate consent for research and ability to rapidly search consent information, we can drive an increase in use.

However, simply achieving a 1:1 utilization rate would amount to a three- or four-fold increase in requests to our research biobank. If we couple on the requirement for more speed, we can expect that it will quickly become difficult to meet demand without automation for ultra-low temperature, discrete vessel, retrieval. The development of such capabilities will have a great impact on scientific research and delivering medicines to patients. Whilst it will force us to rethink many of our processes, we could finally be in a position to lose the “banking” word—it becomes all about using the samples.

Share this ebook!


Fisher BioServices
A Thermo Fisher Scientific Brand