

7<sup>th</sup> December 2018

Dear Customer,

**Update on PET-CT tracer supply**

You may be aware that we have had significant disruptions to our supply of Radiopharmaceuticals during 16<sup>th</sup> – 23<sup>rd</sup> November as well as 4-5<sup>th</sup> December.

While our Keele production facility is shut-down for its dispensers to be replaced, we ordinarily have three other sites that have sufficient capacity to meet demand with around 20% “headroom”. Unfortunately we have had major issues at two of our sites leading to a large number of PET-CT scan appointments needing to be cancelled and rescheduled over the last 3 weeks.

We apologise to all patients affected and recognise the anxiety and upset that a delay can cause.

To explain what happened:

**Sutton production facility (16th – 23rd November)**

- Late on Thursday 15th November a chiller that is essential for the running of the cyclotron broke down
- These chillers have proven to be very reliable in the past and have regular preventative maintenance carried out. This is the first ever incident of a chiller breaking across our 3 sites. The last planned service visit for this chiller was performed on 29th October and no issues were identified.
- Efforts to repair the chiller continued until 19th November when we were informed that it was not repairable and needed replacing
- The chiller was replaced and the Sutton cyclotron was back up and running on the afternoon of the 26th November.

**Preston production facility (19th – 21st November)**

- Following a pre-planned preventative maintenance programme on the weekend of the 17th & 18th November we were notified on Sunday that GE were unable to get the Vacuum working on the Cyclotron with a leak somewhere in the system
- The issue was resolved by GE on Wednesday and Preston was back to being fully operational on 22nd November

**Preston production facility (4<sup>th</sup> – 5<sup>th</sup> December)**

- On Tuesday 4th December the RF tube on the cyclotron failed
- This has happened once before across all of our sites and spares are not maintained by GE in Country
- GE shipped a replacement part in and installed it on 5<sup>th</sup> December and Preston was back to being fully operational on 6<sup>th</sup> December

The immediate steps we took to mitigate this were:

- Flying in batches of other radioactive tracers to allow Guildford, to focus on FDG (Fluorodeoxyglucose);
- Working with PETNET to use any spare capacity they can provide. Due to their own constraints this has been limited to a small number of doses from their Nottingham site; and

- Reducing the radioactive isotope tracer dosage, used in the scans, for each patient to 400 Mbq, where appropriate, to allow for more patient doses to be supplied.

We are working with local site teams to ensure that where patients have been cancelled they are rescheduled and scanned as soon as possible. 90% of patients should be scanned within the next 7 days.

We can only apologise for the significant shortfall in supply over the last few weeks and assure you that we are doing everything we can to restore service to normal levels.

We have been asked a number of questions which I have addressed below:

**What are your back up arrangements in the event of production problems?**

Currently our back up arrangements are that in the event of a supply issue at one of the manufacturing sites, that site will contact the other sites to determine what support is available and sites will then work together to minimise disruption to supply.

If backup supply is not fully achievable within AMR, when we approach PETNET to determine whether they are able to provide any doses, as described above. This is a reciprocal arrangement and PETNET will approach us as and when they have production issues to assist with supplying their customers.

**Can you source FDG from some of the other cyclotrons in the UK?**

Following a meeting with MHRA in September and their formal response in November, we have clarity over when we may source capacity from other non-commercial cyclotrons when there is insufficient capacity from ourselves and PETNET.

Over the last few weeks we have met with four of the non-commercial cyclotron operators around the country to establish what support they are able to provide, with the intention of having some additional capacity in place prior to our Preston facility commencing its shut down. Two of these sites are unable to produce FDG to support, with the remaining two willing to support, but for their own operational reasons are unable to do so before March 2019.

**Why are you replacing the dispensers now?**

The dispensers in the Keele, Preston and Sutton facilities are GE Fastlab dispensers, installed when the sites were commissioned, with the last system being installed in 2009.

We were given notification by GE in January 2016 that our dispensers would become “End of Life” in December 2018 due to some parts no longer being available, leading to a reduced reliability.

Over a 12 month period we reviewed all possible solutions to replace these dispensers, with the only real credible solution requiring a replacement of the associated hot cells as well, necessitating each site to be closed for around 6 months.

GE informed us during 2017 that the dispenser kits would also no longer be being manufactured with a finite number now available. This unfortunately gave us no option other than to replace these units in advance of the kits running out.

An order was placed for these in June 2017 with the equipment ready for installation in spring 2018, with Keele commencing its shutdown period in late May 2018.

The Preston shutdown will commence in March 2019 and Sutton will follow later in the year when Preston is operational again. GE have agreed to continue to support the dispensers during our replacement programme.

**What is your plan to meet the growing demand going forward?**

Alliance Medical Radiopharmacy is committed to ensuring there is sufficient radiopharmaceutical production capacity in the UK to meet the expected growth in demand in PET-CT activity.

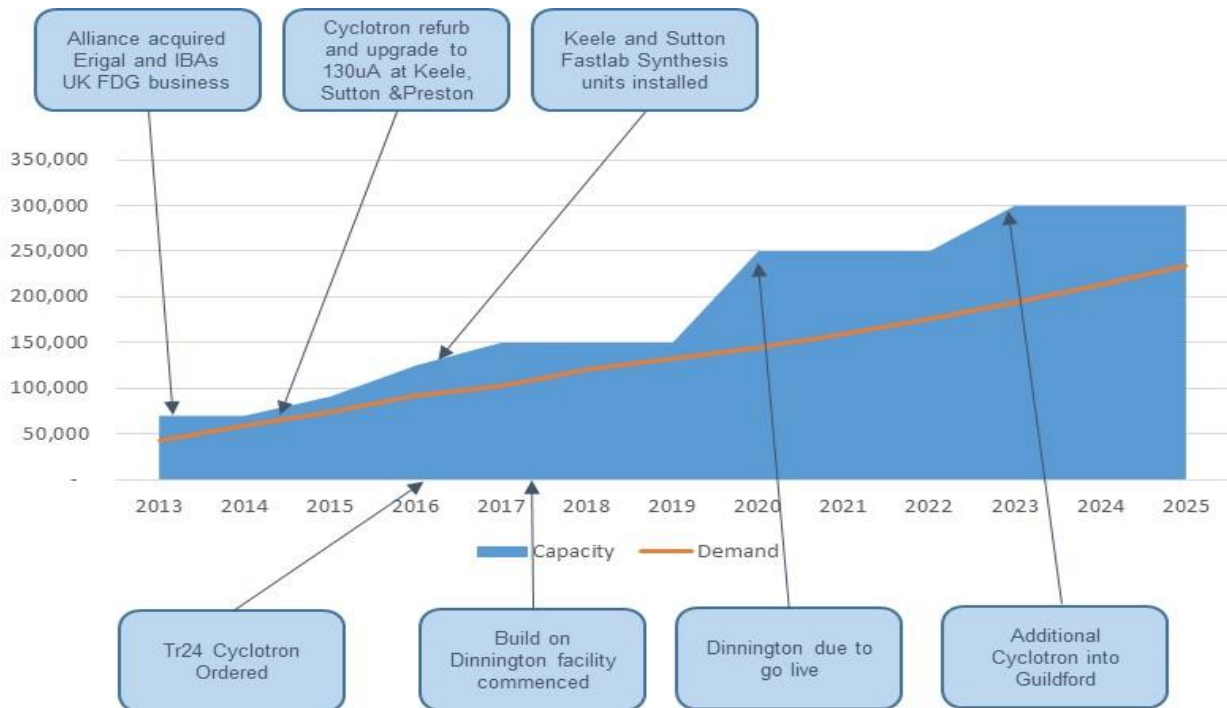
This commitment started in 2013 with the acquisition of both Erigal Limited and IBAs UK FDG business at a time when both businesses were struggling financially and the sites had not been invested in for some time. In 2013 these sites were producing between them around 43,000 doses per annum with capacity of c70,000 doses per annum.

We recognised at this time that the existing capacity would not be sufficient to meet the growth over the medium term and in summer 2014 we started the process to refurbish and upgrade the cyclotrons at Keele, Sutton and Preston to increase their power from 100uA to 130uA, giving a c30% increase in capacity to 90,000 does PA.

During 2015 and early 2016 we also made significant investments to replace and upgrade the synthesis units to further increase capacity to c150,000 doses PA.

In 2015 we committed to re-opening the Dinnington facility, which had been closed by IBA in 2009, and investing in a new Tr24 Cyclotron, which along with the existing cyclotron on site will add significant additional capacity of c100,000 doses PA when it opens in late 2019.

We also plan to install a 2<sup>nd</sup> cyclotron into our Guildford facility, which has a spare bunker, over the next five years to further expand capacity.



I hope the explanations above provide you with comfort that we are doing everything we can do to offer a reliable supply to you in a time when capacity across the UK is reduced as well demonstrate our commitment to providing surety of supply for the long term.

We would also appreciate your feedback on any issues in this letter and ways in which we could improve our communication with you.

Yours sincerely

A handwritten signature in black ink, appearing to be 'H. Marsh', written in a cursive style.

Howard Marsh

Managing Director – Alliance Medical Radiopharmacy Limited