Career Episode 1

Case Study & Analysis of AutoDelfia Abnormal Results

A) Introduction

[CE 1.1] The related details of the accomplished project are:

Title: Case study about the abnormality of result values of AutoDelfia (automatic immunoassay system) in Cheil General Hospital & Women's Healthcare Center

Total Period: 02 Sep. 2015 ~ 15 Sep. 2015

Position: Assistant Manager / FSE (Field Service Engineer)

Dept.: Technical Support Team

Workplace (Company): Bio-Medical Science Co., Ltd. (BMS)

Commented [석이1]: I Put company full name.

B) Background

[CE 1.2] BMS was founded in 1988 and is based in Seoul, and has about 400 staff members in it. This company specializes in researching life science and basic science areas and has introduced cutting-edge technologies and equipment in Korea which are related to medical diagnosis. The company continuously strives to contribute to the development of life science research. And it is now expanding its areas to the development and manufacture of basic research equipment.

[CE 1.3] The project aim was carrying out the detailed maintenance and repair service on the prenatal&neonatal diagnostic equipment which the technical support team of BMS performed where I am a part as an FSE (Field Service Engineer). The purpose of this episode is to examine the process of how I, as an FSE, managed to solve the abnormality of result values produced from the AutoDELFIA equipment (medical diagnostic equipment) capable of screening congenital diseases such as Down's Syndrome, hepatitis, and thyroid disease, and to look into how I applied my expertise in electronics and electricity in solving the abnormality. In this particular case, I received the call about the abnormality of result values of the equipment and participated in this case for the first time as a field service engineer.

Commented [석이2]: I corrected the vocabulary.
Fetal -> prenatal&neonatal

Commented [k3R2]: Alright.

[CE 1.4] In the project, the equipment in question was relatively antiquated one which has been used in the hospital for 7 years now since its initial installation, and about two months have passed since it last received the regular quarterly preventive maintenance. The number of samples in this hospital was relatively small, compared to that of other hospitals, and its backup equipment was not installed. The equipment concerned was in an operable condition, but it continued to produce untrustworthy results without having a consistent pattern from the particular wells of the micro plate.

[CE 1.5] The hierarchy for the project position representation:

[CE 1.6] My relevant project duties were:

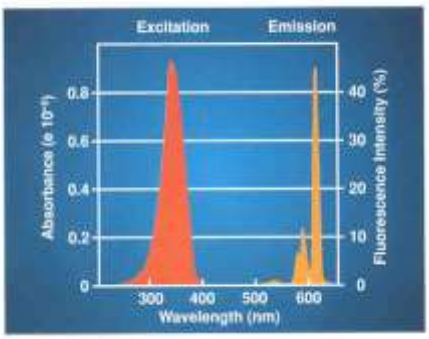
- I applied biomedical engineering skills for storing the reagents conditions including buffer, tracer and enhancement solution.
- I did the upgrading of the second-generation vacuum along with the pressure pump which worked in the third-generation version.
- I conducted XY coordination calibration for detector and obtained the parameters which were not similar to the under-considered parameters.
- I examined the emission filter position in the machine utilizing my biomedical engineering expertise.

Commented [석이4]: I added "for detector"

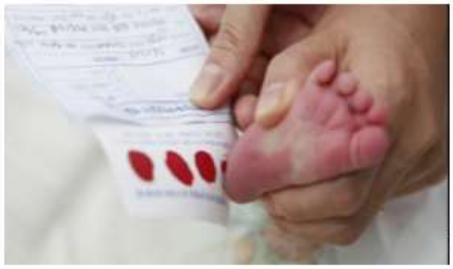
Commented [k5R4]: Alright

C) Personal Engineering Activity

[CE 1.7] The equipment of this case processes a serum (prenatal screening) test and a DBS (dried blood spot)-based neonatal screening test. Also, the equipment produces measured values by scaling the electric signals collected through amplification and detection of photon signals in a PMT (photomultiplier tube) which are measured and counted in the antigen-antibody reaction and fluorescence detection of samples. Though the measuring method was similar to fluorescence intensity (FI), a TRF (Time-Resolved Fluorescence) technology was used in this case which is a method of increasing excitation time.



[CE 1.8] Once a user finishes placing a blood disk on a micro-plate which is made by punching a paper soaked with a baby's blood in a specific size, the equipment automatically takes care of all the other operation until it produces results. In other words, the level of a user's skills has little to do with the results of an experiment. However, this kind of fully-automated equipment has many moving parts inside so it is necessary to get a maintenance and repair service from a certified engineer regularly. Abnormality of this equipment's result values can be examined first from the exteriors of hardware as is typical with any diagnostic equipment. By doing this first, a possibly unnecessary job of disassembling the equipment can be avoided and a lot of time is saved. If a sample was chemically transmuted, or not enough amount of blood is soaked into dried filter paper cards when collecting a sample, the result values were abnormal. The conditions under which samples were stored such as temperature and humidity and the amount of blood in the dried filter paper card was checked with naked eyes. Also, if the person who collected blood gathered not enough amount of blood onto the front and back sides of a dried filter paper card, inaccurate data was produced. Other than these factors, I checked the storage conditions of reagents such as a tracer, buffer, and enhancement solution, and their expiry dates.



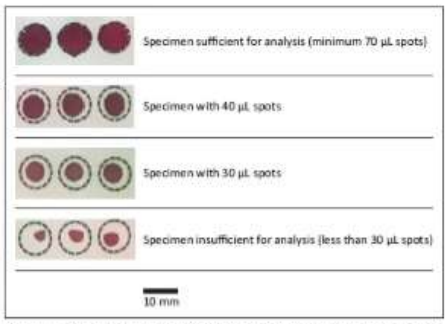
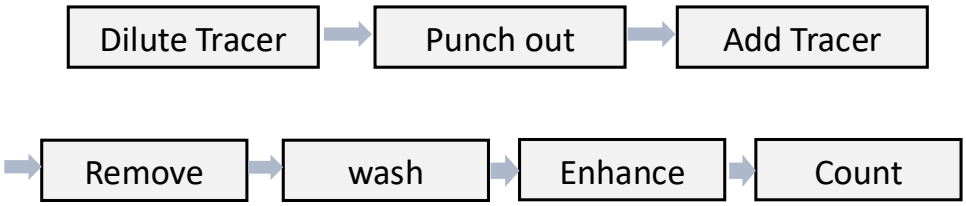


FIGURE 1: Example filter paper card with sufficient and insufficient blood spots.

Because abnormal results of data have to do with all the procedures of pre-processing that deal with samples, it is important to first grasp the order of operation inside the automation equipment and then inspect it in tune with its operational orders. This strategy was to save time and for ensuring that no inspection items were missed. This particular case concerned the result of a neonatal screening experiment, and its process is as follows:
<Neonatal Screening Process>



[CE 1.9] I decided that I performed the preventive maintenance one month earlier than an original date because this maintenance included the work on most of the parts involved in the operational orders of the equipment. Furthermore, I decided to also upgrade the second-generation vacuum & pressure pump into a third-generation version. This preventive maintenance was largely composed of four sections. It is summarized below.

- Replacing expendable components and cleaning / replacing or calibrating the parts with a replacement cycle and those that did not match their specifications when conducting a performance test, and cleaning, sterilizing and applying magic oil to the equipment exposed to users and samples / related parts: air filter, filter for wash, rinse bottle, and Pipettes**.**
- Calibration work, cleaning, and applying lubricating oil to the moving parts / Most of the moving parts may malfunction when their limits of margins of error are exceeded with the accumulation of step errors as experiments are repeated without interruption. / X-conveyor, Lift, Washer, Enhancement Dispenser, and Remover**.**
- Work on parts related to temperature / three units of Peltier is installed inside the equipment to maintain a constant temperature of the incubator that is stored while shaking samples and in the equipment. And three temperature sensors are installed which detect the constant temperature. Inspect whether the Peltier and the temperature sensors are working properly. / Cooling units, temperature sensors**.**
- Check the injection amount of fluids / it is required to take and inject an accurate amount of reagents / Pipettes, Washer, Enhancement solution dispenser**.**

[CE 1.10] All the calibration works were performed after replacing the necessary components. All the moving parts moved around the location parameters where they were stored on EEPROMs of LCC controller boards. After performing the replacement work, I revised those parameters needed to the newly calibrated values. And before all the maintenance works started, I stored the parameters on all of the EEPROMs which must be made a backup.

Commented [석이6]: The equipment in question was within one month before it gets regular preventive maintenance. And I decided that I performed the preventive maintenance one month earlier than an original date because this maintenance included the work on most of the parts involved in the operational orders of the equipment.
(!) **I deleted the yellow part. Please tell me if this can be read awkward.**

Commented [k7R6]: This looks alright.

Commented [석이8]: **(The image in the [CE 1.10] is about "upgrading pump, 2nd generation to 3rd generation, but this paragraph didn't have any context about "pump", so I added it,,, and I tried to reduce some words. Let me know if there are some awkward parts.. 😭)**

Commented [k9R8]: It is ok. I have added changes too.

Fig. Second-generation pump set

Fig. Third-generation pump set

The reason why 2nd-generation pumps are ungraded to the 3rd-generation pumps is because condensed water is generated and it flows backward the pumps, thus shortening the longevity of the pumps. Performance of one of the three vacuum pumps is weakened, which noticeably reduces the longevity of the other two pumps. In order to prevent these problems, tubing is curved before it is installed, but there are reports that water still flows into the pump because the location of tubing is changed due to vibrations made when a suddenly high pressure is applied to the tubing because the tubing is not fixed securely. So, I developed the third-generation pump set and supplied. Overall, I noted the improvement in the performance, and the curved tubing for preventing water from flowing backward was fixed securely on the rear side of pumps so the problem of changing positions of tubing due to vibration was solved. Because the cable connected to the connection board and the power supply was changed, I installed an upgraded connection board (upgraded connection board was pointed by a finger in the figure of 3rd generation pump).

[CE 1.11] Samples (micro plates) were moved to measuring unit (detector) by lift after the pre-processing. I cleaned and applied lubricant to X and Y axes rail of measuring unit and calibrated coordination with special tool called “a search plate”.

Commented [석이10]: Please check any grammatical Error in this paragraph because I added this paragraph.

Commented [석이11]: Please check any grammatical Error in this paragraph because I edited this paragraph to reduce word counts. 😊

After the pre-processing of all the samples is finished, microplates were moved by the lift to the measuring unit for detection. The measuring unit was formed as a darkroom to prevent noises from entering the sensitive PMT. A conveyor was inside the measuring unit, which moves in the directions of X and Y axes along a rail, therefore each well of the microplates needed to be adjusted to apertures so they can be counted. So, first and foremost, I cleaned the rails of X and Y axes, applied lubricant to them, then conducted a mechanical test, and confirmed that all the values of operation were performed within the allowable speculations. By using a tool called a search plate, I performed an XY coordination calibration and found out that parameters are not much different from the previous parameters.
-> Samples(microplates) were moved to measuring unit(detector) after the pre-processing by lift. I cleaned and applied lubricant to X and Y axes rail of measuring unit and calibrated coordination with special tool called “a search plate”.

Fig. Search Plate – it is used in a measuring unit to calibrate the positions of microplates so that they can be lined up for detection

In the process of the biannual preventive maintenance, I additionally examined the position of an emission filter and obtained a result as below. Ideally, only one highest peak value should be produced and in the part of a light shutter, i.e., the part with no filter, the light should be blocked and counted as near zero. With the result below, I decided that there is a problem with light leaking or an emission filter changer itself has problems. So, I held a video conference twice with the engineers of the manufacturer of the equipment to find out what kind of additional inspection should be carried out. They suggested that I should replace the entire measuring unit, but there were a number of problems about that: the measuring unit is expensive; the customer has to wait for a long time because currently there was no stock left, and our sales team and my colleague engineers in our company gave me their opinions that it was not viable given the break-even point of the measuring unit. Therefore, I decided to perform the re-calibration of discriminator levels and carry out the inspection of the emission filter set for repairing the measuring unit itself.

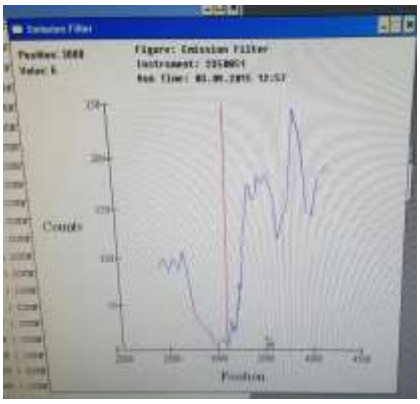


Fig. Result of the Emission Filter changer Test

[CE 1.12] By discriminator level, it meant a level of no noise and it was set up to improve an SNR (signal-to-noise ratio) and prevented the drift of data. An oscillating circuit was used in the high-voltage power supply circuit which was connected to the PMT that acts as a detector, and here unwanted noises are generated from an output terminal which was called a ripple. If a threshold of the discriminator was established higher, a rate by which a little change in an input terminal influences results values also rises. Therefore, I worked on establishing the threshold which was being higher than noise and lower than a signal. For this equipment, an oscillation level should first be found. Then the oscillation level plus 10mV was established as the discriminator level. After finishing this setup, I established the filter position of the measuring unit and flash rate calibration of a light source and other works were performed.

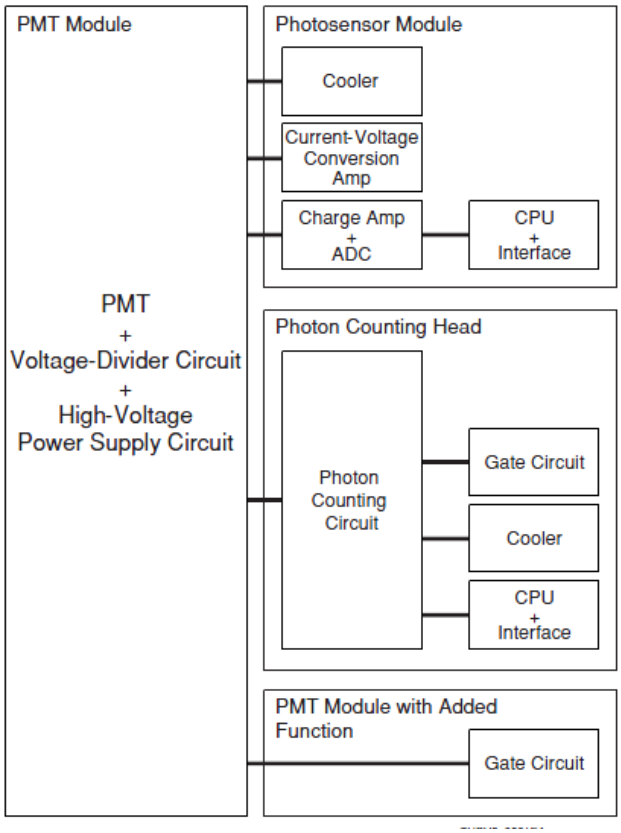


Fig. PMT with High-Voltage Power Supply Circuit

After I finished the set up in the discriminator, I was able to find the position where a count value is almost zero at the step/stage of defining an oscillation level. And this means there was almost no light leaking. In other words, it looked like the possibility of leaking goes higher when the positions of filters were changed. The emission filter has four positions in it in total, and it comprised the parts of Sm (642nm), Tb (545nm), Eu (616nm), and Light Shutter (a blocked part with no filter). And it was connected to a step motor so that the position of a filter can be adjusted to the type of a label. When I performed the position calibration of the emission filter repeatedly, I found out that the resultant graph forms of counts were not consistent and that the step motor was unusually overheated after it began to operate. I could assume that the antiquation of the step motor itself or the abnormality of an LCC board that controls the step motor has caused the malfunction. I could also presume that intermittent malfunctions of the step motor prohibited a light shutter from being perfectly closed and thus may cause the production of untrustworthy random result values. Though the price of a step motor was inexpensive, if I replace it with a new one when the operation of the LCC is still in error, the new step motor will be adversely affected by it. Also, it is difficult to allocate more time to the troubleshooting because currently, the customer has many overdue samples of patients that need to be examined. Therefore, I decided to replace both the LCC control board and the step motor at the same time. After securing a backup of the parameters of this LCC board, I installed a new LCC board and then entered the parameters.

[CE 1.13] After carrying out inspections and repairs of all the devices and equipment, engineers confirm whether all the count values would meet the recommended speculations of a manufacturer by using a 1nM Europium which is one of the Tracers. 200 µL of Europium would be injected into each well, then count values are read in service mode. Reagents could be evaporated so pipetting should be performed as quickly as possible within 15 minutes. Also, because reagents are sensitive to lights, this mission needs to be carried out in a dark room. And reagents on the microplate should be covered with foil and then carried to the equipment. To manually handle machines, engineers need the practice of pipetting at the same level as researchers. After conducting a Europium test, I confirmed that all the count values satisfied the specifications. After writing a service report and a Europium certificate, all of the inspections and repairs I have performed were completed.

D) Summary

[CE 1.14] All types of equipment made for research and/or diagnosis have an error log in them. All the obvious mechanical (hardware) malfunctions were recorded on an error log, and in this case, the equipment stopped operating to prevent samples, reagents, and expendables from being wasted. Therefore, these kinds of the problem were relatively easily examined based on the records of the error log (troubleshooting). However, I noted that these were complicated to solve cases like this one because there were no apparent mechanical problems so the equipment was able to produce the result values but which turned out to be untrustworthy. Because the diagnostic equipment would mainly use in hospitals, providing accurate and quick service was very important. If a problem gets complicated like this issue, it was vital to identify how the equipment was used

Commented [석이12]: (I deleted yellow parts. Please check if it can be read awkward. 😊)
To manually handle machines, engineers need the practice of pipetting at the same level as researchers. After conducting a Europium test, I confirmed that all the count values satisfied the specifications. After writing a service report and a Europium certificate, all of the inspections and repairs I have performed were completed. After that, the customer began to conduct a test for samples on the spot and I watched the whole process of the test until the first result of a sample was produced. Compared to other cases, this case took a long time, so the customer's anxiety level was great.

Commented [k13R12]: It is ok

in terms of pathology, then to set priorities according to the information about its usage after simulating its operational orders, and to understand the issue in stages. Occasionally, there were cases where I was needed to decide the scale and degree of repair, depending on the status of parts in stock and the business circumstances with a customer. My bio-medical engineering knowledge significantly boosted with the objectives completed in this project.