REGION H Rigshospitalet

PET & Cyklotronenheden

Technical documentation and risk assessment for Tracershop

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Introduction

This document describes the electronic web shop, Tracershop, used for ordering and release of radioactive tracers for clinical and pre-clinical procedures produced at Rigshospitalet's Cyclotron and radiochemistry unit. Since radioactive tracers are medicinal products, Tracershop must fulfil documentation requirements stated by GMP Volume 4 annex 11, which this document describes.
Rigshospitalet delivers radioactive PET tracers to hospitals and scientific institutions around Copenhagen. It would not be possible to perform PET scans without these tracers. Therefore Tracershop should be considered a important piece of software.
Tracershop was released in 2004 and is used to this day. Due to it's age a new system have been developed with the intent to replace the old system. This document contains a short description of the old system, then a deeper explication of some techniques and technologies that the system is using to obtain a "Better" software product.
Since annex 11 is dated, EMA has released a concept paper on annex 11[1] containing various comments on the guidelines presented in annex 11. These comments have also been considered when applicable.
The document have been review with Jacob Madsen as Production chief and Helle Østergren Bak as Quality Assurance, and Christoffer Vilstrup Jensen as developer.

User Requirements

The requirements of the software, that tracershop fulfils are:

- A shop user can order radioactive tracer on behalf of a customer, which have been certified to the ordered tracer.
- A shop user can view any order that been have made to a customer they are associated with.
  They can view batch numbers of any product that they have received.
  They can delete orders, that have been requested, but not accepted or released.
  They cannot alter accepted or released orders.
  They cannot view orders from users that they are not associated with.
- A production user, that have been certified can release a radioactive tracer.
- Production admin can grant and remove certification of other production users. A production admin user cannot grant any rights to themselves.
- A released order has a batch number and a record of who released it.
- Non authenticated users cannot alter or view information in tracershop.
- A released tracer must display if it's intended for preclinical usage or human usage.

Terminology

Tracershop handles two different types of orders. Activity based orders and Injection based orders.
An **activity order** is defined as: An order, where a customer orders an amount of MBq radioactive tracer at a predetermined time slot known as a "deliver time". It's the user responsibility to account for radioactive decay between injection time and delivery time. Delivery time slots are determined by the production users and are allocated per user.
An **injection order** is an order with a number of injections with a predefined amount of activity, and it's Tracershops responsibility to account for any radioactive decay between production time and injection time.
Users er limited which injection tracers they can order, determined by the production users.

Tracershop - Current system

The software ecosystem is centered around a MySQL 5.1 database running on a openSUSE 11.2 distribution, which contains all the records and logs about the production of tracers. This database is back up on an external machine every day at midnight.

Tracershop is a web site hosted with Zope 2-2.13 web interface at http://pet.rh.dk allowing the users to systematically write to the main database. These messages are logged.
The website is deprecated and no longer receive updates. The system contains an dispenser, that records how

[1] https://www.ema.europa.eu/en/documents/regulatory-procedural-guideline/concept-paper-revision-annex-11-guidelines-good-manufacturing-practice-medicinal-products_en.pdf

much radioactive material was dispensed, allowing accurate tracking of activity in vials and minimizing human error. This data is pushed via a script to tracershop.
An overview of the current system can be seen in figure 1.

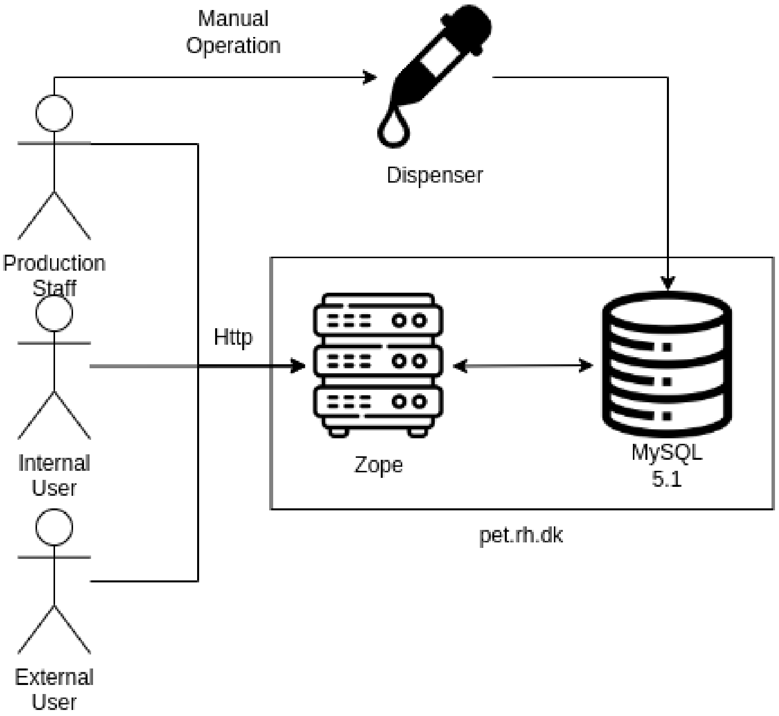


Figure 1: Current Tracershop system

The system is hosted on internal server owned by The Department of Clinical Physiology and Nuclear Medicine. This is not desired because hosting server is a core task for CIMT and not for the clinical departments.

Database layout

The database contains the following tables:

1. Log - Likely Zope related. No longer in use as the last entry was in 2010-03-18.
2. MiscData - Likely Zope related. Likely a temporary value container.
3. Roles - Zope related, defines different user roles in the Tracershop program.
4. Sessions - Likely Zope related, defines active user sessions.
5. Tokens - Likely Zope related, Likely defines the length of active sessions.
6. TracerCustomer - Defines which user have access to order which injection Tracer.
7. Tracers - Catalog of tracer available in tracershop.
8. UserRoles - Relates user to a Role from the Role table.
9. Users - All users able to be authenticated in tracershop
10. VAL - Record of a vial with tracer, produced by the dispenser.
11. VAL2 - Not in use.
12. blockDeliverDate - Extraordinary dates where tracershop is closed, such a holydays.
13. deliverTimes - Weekly points in time specifying when a customer can place an activity order.
14. isotopes - Catalog of radioactive isotope used in the tracers.
15. orders - List of activity orders.

16. productionTimes - Weekly points in time, where a production should happen. Entries are also referred as a run.
17. productions - Production of tracers.
18. storage - Old mails, assumed not in use.
19. t_orders - List of injection orders.

The database is not utilizing the foreign key restriction, meaning that the relations are ensured at application level and not the database level, and as such only reaches the first level of database normalization. This low level of normalization allow a number of error to be present in the database:

- Reference errors - When a field references another table without the foreign key restriction, then the reference can point an entry that doesn't exists, which is a error, therefore any change to an ID, must by application logic update the rest of database.
- Transitive functional dependencies may not respected. As an example: An activity order contains both the amount of radioactive material was ordered and how much tracer should be produced while taking into account the overhead percentage of the customer. If the ordered amount is edited then the database integrity relies on application logic to update overhead amount.

It's considered an industry standard to keep databases in third normal form, which require the database to be designed in such a way, that these errors cannot occur.

The new Tracershop

For the rest of the document, the name Tracershop will refer to this solution. The setup for Tracershop can be seen in figure 2. It's a virtual computer hosted by CIMT running Red hat 8 https://www.redhat.com/en:

plnxtshop01.unix.regionh.top.local - 10.146.12.175

The server run the following programs:

- F5 - This is reverse proxy web service, managed by Net design. It's responsible for forwarding http and ws request to Tracershop.
- Apache - open source web server, https://www.apache.org
- Daphne - Websocket protocol server, developed for django channels https://github.com/django/daphne
- Vial Fetcher Service - This is a small program responsible for fetching data from the dispenser, however since the dispenser is only able to dispense files, a network drive is an intermediate link.
- MariaDB - Open source Mysql database - https://www.mariadb.org
- Redis Database - Open source in memory database - https://www.redis.io
- Supervisor - Monitor program for Daphne http://www.supervisord.org
- Ping Service - This is a hl7 message server, that will receive bookings with relevant tracers, this allows shop users to automatically order tracers based on incoming bookings.

The underlying web service is an open source django / channels web server found at https://github.com/demiguard/Tracershop. It's developed and maintained by Christoffer Vilstrup Jensen.

The tracershop uses common software packages for web servers:

- React - Frontend Javascript library developed by facebook. https://reactjs.org
- Django - Backend Python web server library https://djangoproject.com
- Channels - Django extension for using websockets. https://channels.readthedocs.io./en/stable

These packages are well supported and all in active development, so their developers will continue to provide security updates. Because these packages are commonly used, it's easy to find a replacement developer, should the current developer leave Rigshospitalet.

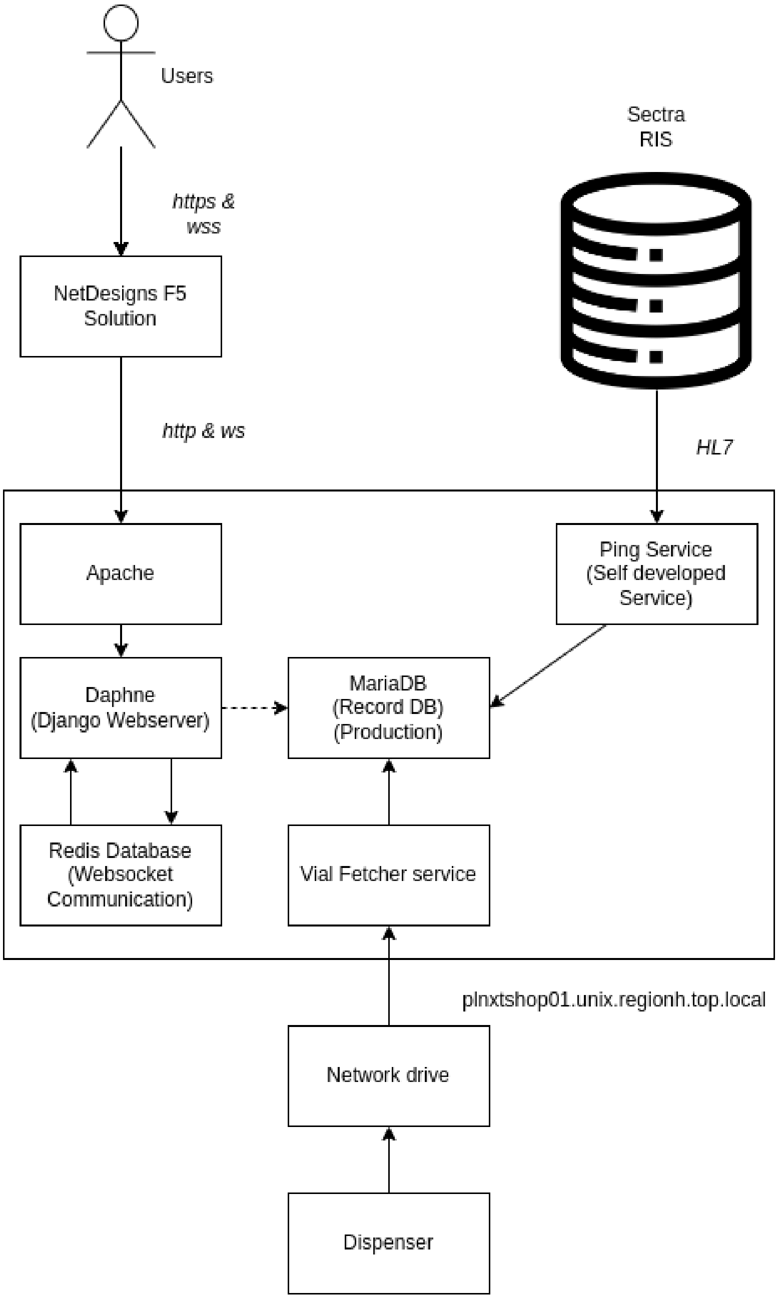

Users
https & wss
NetDesigns F5 Solution
http & ws
Sectra RIS
HL7
Apache
Ping Service (Self developed Service)
Daphne (Django Webserver)
MariaDB (Record DB) (Production)
Redis Database (Websocket Communication)
Vial Fetcher service
plnxtshop01.unix.regionh.top.local
Network drive
Dispenser

Figure 2: The new system

Message handling

Tracershop utilize websockets instead of purely http communication, because websockets allows the server to push updates to the users unprompted, because the protocol uses a persistance connection, while http does not use a persistent connection. This technology allow the communication protocol seen in figure.

1. A user causes an update, that needs processing from the server.
2. A message is send by the server
3. The message is processed by the server
4. the server sends a responses, that the message have been processed. If the message type require an update websites state, then the server informs all clients by broadcasting the message.
5. The server rerenders the website with the modified state in mind.

To ensure that each message is valid, and that user is authorized to send that message, all message are processed in a three step plan seen in figure 4

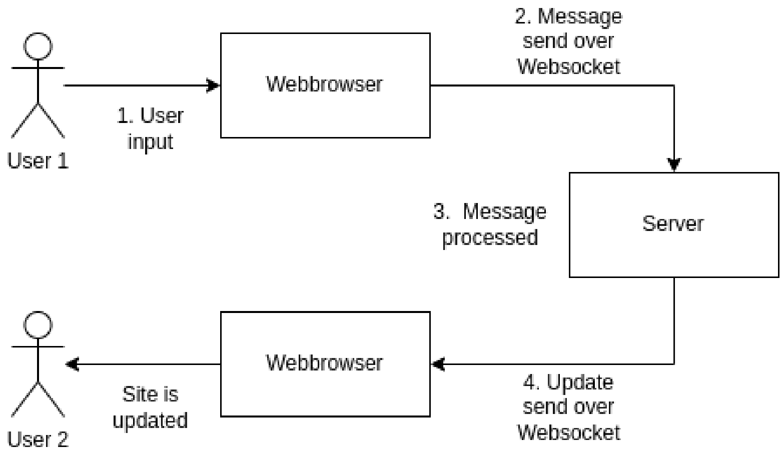


Figure 3: Overview of the message handling.

1. Validate message - The server determines if the message has all the needed fields and that the fields contains values of the expected type. It also ensures that sender doesn't have an outdated version of the frontend client. If validation fails, there's no update to the database.
2. This checks that the sender is authorized to send, this message type. If authentication fails, there's no update to the database.
3. Message processing, this step performs the message.

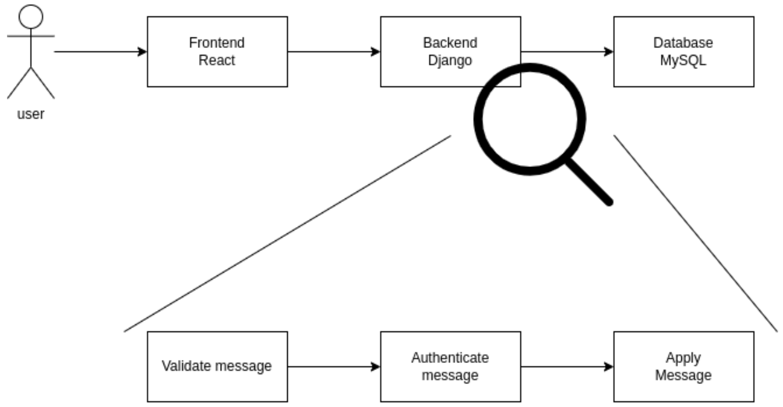


Figure 4: Message handling by the backend

New login system

The new tracershop system uses an external authentication system, provided by the Capital region called BAM ID, managed by CIMT. All members of staff working in the capital region have a BAM ID login.

This login have various security features build in, such as automatic deprecation of passwords, password reset, deactivation of inactive accounts, and minimum complexity requirements to passwords. CIMT also handles reestablishment of forgotten passwords. Secondary tracershop doesn't need to store passwords and instead store tokens that the system can authenticate against CIMTs systems.Consequently if the system is compromised, no data about the users passwords can be leaked.

All users in Tracershop are personal and have a role determining their rights. A user can only have a single role. These roles are divided into a Shop- or Production category. Shop users are representatives for a customer organization, that uses products from Tracershop. Production users are members of Rigshospitalet Cyclotron and Radiochemistry unit and releases tracers in tracershop.

If a user is a staff member of the Capital region they acquire their role by contacting the local active directory manager (CBAS administrators), requesting the role. The manager can then determine if the role that is requested is appropriate and accept or deny the request based on their judgement.

All the roles are as follows:

- Shop - External - This user is related to a customer, which is not part of the capital region. The user isn't an employee of the Capital region and doesn't have BAM ID, therefore their profile cannot be managed by CIMT or benefit from automatic ordering. They can view their assigned customer's orders and order tracer authorized to the customer. Each of these user are connected to an external customer. The user is managed by an production admin.
- Shop - Internal - This is an employee of the Capital region and therefore have a BAM ID. A user is associated with one or more internal customers. This user is managed by a "Shop Superuser" user.
- Shop - Superuser - This is an internal shop user with additional rights to modify the automatic generated order based on a RIS booking. They can grant an internal user access to the same customers that they moderate.
- Production - User - The user can view and accept orders from all customers. They can release tracer of authorized types.
- Production - Admin - Everything the production user can. Grant release rights to other production users, create new tracers, allow tracers to be ordered by customers, and manage external users.
- Site Admin - The equivalent of a root user. The user can mimic all the functionality of other roles. The user isn't intended to use tracershop only to support it.

In addition to the user role, tracershop keeps track of which user can represent which user. If a shop admin user represent a customer, they can grant other shop internal users the right to represent this customer.

Logging

Annex 11 is very light on it's requirement of logging, therefore we refer to the comments in the concept paper. [2] The raw logs are only accessible by system administrators. Each log entry has a time stamp, and a record of the user which invoked the user statement. Anonymous users cannot trigger log actions, because they are filtered away by the F5 reverse proxy.
The new tracershop contains the following logs:

- Audit log: The audit log contains significant actions related to GMP. The log is permanent (not rotating), and is backed up at the same level as the server. The following actions are log in the audit trail:
  - The system automatically assign or reassigns: the Shop Superuser, Production Admin, or Site Admin user group to a user.
  - A production user / admin manually adds a vial, data of the vial is logged.
  - A production user / admin manually edits an existing vial, the old and new data is logged.
  - A production user / admin releases an order.
  - A production user / admin edits a released order. The old and new order data is logged.
  - A production admin / Site Admin grants releasing rights to a production user.
- Operational web service Log: General operational messages - Indented for debugging. Weekly Rotating log, 4 weeks of logs are kept.
- Operational ping service logs: Logs generated by the ping service. Weekly rotating log, 4 weeks are kept.
- Operational Vial fetcher service logs: Logs generated by the vial fetcher service. Weekly rotating log, 4 weeks are kept.

Correctness of Tracershop

Ensuring correct behavior of any program is a difficult process. Errors increase proportional to the complexity of the system, interactions with other systems and changes to the software ecosystem.
To combat errors an automated test suite have been developed. These tests can be divided into three parts, an predefined arrange state, an action to be performed and finally an assertion about the result of the action.
A well developed test suite has the benefit of making changes easier to implement correctly because they display any cascading impact of any changes.
A test covers a line of code if that line of code is executed in the test. From this term coverage of a test suite

[2] https://www.ema.europa.eu/en/documents/regulatory-procedural-guideline/concept-paper-revision-annex-11-guidelines-good-manufacturing-practice-medicinal-products_en.pdf

is defined as the percentage of lines covered by all tests of the suite.
Recommended percentage of code coverage is a greatly debated topic in the software development communities. The main debate revolves around the last 5-10 percentage points of code coverage. This is because these lines of code often handle edge cases, are unreachable or handle faulty connections to other sub systems.
High code coverage can also lead to rigid code bases, slowing down development of new features. Full test coverage doesn't prevent software related errors from occurring. Tests are also not free, as they take time to develop and maintain. The author recommend a 90 percentage code coverage.

Software tests doesn't reduce human errors, but can be reduced by various sanity checks, that can be performed automatically. Nor does they prevent other subsystem from failing.

Risk assessment

Tests can by definition only showcase that the program works in a predefined "idealized" environment nor do they deal with incorrect data. To combat the problems uncovered by the automated testing. There has been made a risk assessment below.
A risk assessment is a collections of risks, where each risk consists of:

- A description of the risk.
- A highlight of the current system
- A likelihood of how likely an incident is to occur.
- A damage estimate of an incident.
- A plan of action if an incident happen.
- How the new system reduces this risk

This risk assessment doesn't include production related risks such a dropped vial, or tracers not passing quality control.
The dispenser and the program transferring data have not modified by the new Tracershop, and therefore derives its validity from previous risk assessments. See document number.: PVP-PROD-Tracershop-001-14.01 in D4, for the latest validation of Tracershop.

- Loss of a server.

Description - A hosting server might become unavailable for of number a reasons: A foreign threat might encrypt the entire server, hardware failure, or a critical files might become corrupted due to aging hard drive. This is not an exhaustive list of reasons for server loss however other factors have minimal likelihood. It's beneficial to have plan of action in the event of an incident caused by an unknown risk.

Currently - Currently the service runs on old hardware, insecure protocols and outdated software, which raises the likelihood of an incident occurring.

Likelihood - Low to medium, Likelihood is increasing with age of the system.

Damages - High - Without the server, it would be impossible to create electronic records of produced tracers.

Plan - Repairing the server hardware might be possible and could restore the system to a pre-incident state, within 1-5 working days. If that's not possible to repair a new server is required. Assuming that the system is not deployed on CIMTs services and a spare server is not available, procuring a new server would take between 4-12 weeks with a 1 week installation period afterwards.
Any data not in the backup would be lost.

New System - The system is hosted by CIMT, in a virtualized environment, allowing for easy cloning and therefore a short the recovery period.

- Database is brought into an invalid state or incorrect state.

Description - Due to the fact that it's the application responsibility to ensure correctness of the database, this is a risk of incident.
If the record database is in an invalid state, undefined behavior might occur because some data is invalid.
Consider an example where a tracer is deleted. All orders with that tracer can no longer be determined to be of that tracer.
A common source of errors have been duplicate acceptance messages, this have causes orders appear released. In the new tracershop, both accepting and releasing orders are idempotence operations.

Currently - If the database is in an invalid state, the site is unavailable.

Likelihood - Low - The web services doesn't allow, the user to perform arbitrary SQL queries, only predefined queries that take the database from one valid state to another valid state. It's difficult to ensure all possible user inputs, so it's possible that a user query might bring the database into an invalid state. An incident could occur if a system administrator creates a query that brings the database is into an invalid state.

Damages - None to Low - Restoring the database is an easy task for a system administrator, worst case would be to revert to a backup. If the invalid state persist unnoticed for more 1 day the backup will be over written and the damage made permanent.

Plan - Upon notice a system administrator would enter the database and create a query to revert the database into a valid state. All queries made by tracershop to the record database is logged, which can greatly help system administrator to undo the damage. If the system administrator unable to restore the data using a query, then the plan switches to rollback to a backup of the record database, causing 1 days worth of data loss.
Note that direct queries to the database is not logged to the audit log, therefore their actions are untraceable, similarly their edits might not record the previous data, that is required to be logged.

New system - A new database has been designed to be on fifth normal form, eliminating reference and transitive errors, making it impossible to bring the state in an invalid state. A page for unexpected errors has been created, giving some hints to what the error might be.

- Incorrect user input

Description - Tracershop have a number of fields, where the user must write some data in. Most critically this includes batch numberBecause it's humans that write this data, the system is subject to human error. It's incredible difficult to prevent this as there's nothing inherently wrong with incorrect data user input. This also includes whenever a user forgets to update a piece of data.

Currently - No warnings are given when attempting to release an order from another day.

Likelihood - High. Humans use this program, no further elaboration required.

Damages - None to High - Not all data in tracershop is critical, however if incorrect batch number is written to the database and the error is not noticed, then that could put patient safety at risk. If the incorrect data is auxillary, then there's no damages.

Plan - If the data is committed, a system administrator must edit the data, if not the data can be edited in tracershop. The new system allow user to edit incorrect of non critical entries.

New Systems - Additional warning has been made for commons errors, like freeing orders from the wrong date. See figure 5.

- The dispenser script stops working

Description - The service that provides information on the tapped vials consists of many different machines which introduces some fragility, as if any of the links of the chain fail, the entire service fails. These are:

  - ∗ The computer connected to the dispenser
  - ∗ CIMT network drives.
  - ∗ The Tracershop main service.

Currently - The current system only allows for the dispenser to be used with FDG, the new system can use this system any number of tracers.

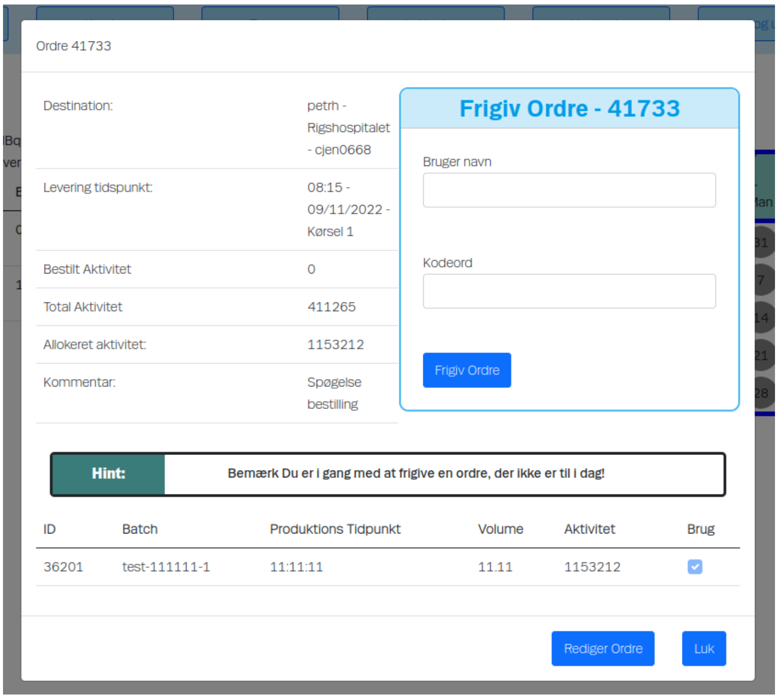
Likelihood - Low - While there's many links, two of them are of high reliability. Namely the network drive and the web hosting server. These servers are prioritized by CIMT to keep up. The final computer is connected to the dispenser. While it's unlikely to fail without changes, however if this PC would become a CIMT controlled PC, then it would be subject to various updates, that might break the programs running on the PC. If the computer controlled by CIMT likelihood increase to medium.

Damages - Low - Vial data can be written by human. This introduces human error and falls in under the risk of human error.

Plan - Users would be forced to manually input data, that normally would have been transferred automatically and correctly.

- Email server is unavailable

Description - The email service is external, thus may for any reason be unavailable for an undefined amount of time.



Ordre 41733

Destination:	petrh - Rigshospitalet - cjen0668
Levering tidspunkt:	08:15 - 09/11/2022 - Kørsel 1
Bestilt Aktivitet	0
Total Aktivitet	411265
Allokeret aktivitet:	1153212
Kommentar:	Spøgelse bestilling

Frigiv Ordre - 41733

Bruger navn

Kodeord

Hint: Bemærk Du er i gang med at frigive en ordre, der ikke er til i dag!

ID	Batch	Produktions Tidpunkt	Volume	Aktivitet	Brug
36201	test-111111-1	11:11:11	11.11	1153212	☑

Figure 5: Modal for releasing an order

Likelihood - Unknown - The author have so limited experience with the available of the mail server, that a valid likelihood estimate is difficult to make.

Damages - None to low - Customers are required to wait for confirmation that the tracer passed quality assurance mandated by GMP, so if the email server is down, the customer can not be notified through email.

Plan - Delivery bills can be send via mails, phone calls and other communication.

New system - The users can download delivery bills in new system, emails are deprecated and will shut down.

- Malicious usage of tracershop

Description - A user of tracershop attempt to sabotage the site. This risk also includes impersonation of staff members.

Currently - All communication is unencrypted, the service is vulnerable to SQL injections.

Likelyhood - Minimal - Users both staff and customers are verified users, which minimizes the risk of malicious usage.

Damages - Low - Even in the event of that a user some how manages to destroy the record database, the backup is stored externally and thus not subject to any attack by the malicious user.

Plan - All account are Personal. Critical actions such as freeing orders are audit logged. Allowing system administrator to identify the malicious user. There's a detection of SQL injections before the execution of each query, if it detects an injection it discards the query.

New system - Security holes with SQL injections are patched. Communication is sent over encrypted channels.

Conclusion

The new system contains substantial upgrades to user experience, IT security, and functionality. It fulfil the requirements stated by GMP Volume 4 Annex 11