Technische Universität München

*Documentation*

# Providing Corona diagnostic consumables locally, cheap, and reliably

Tech Challenge
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# 1. Introduction of Challenge

The Bio.Kitchen is an open community lab from the UnternehmerTUM. They offer tools for rapid prototyping and courses in the field of biotechnology. Together with the Gesellschaft für Internationale Zusammenarbeit (GIZ), they develop a mobile Corona diagnostic lab that allows testing in third-world countries. The first pilot-project of these mobile stations will take place in Ghana. As of today, one challenge is that the market for diagnostic plastic consumables is exhausted and prices exploded. It is estimated that the costs of consumables for 300 Corona tests are of around €3,250. Therefore, we worked on a solution to provide Corona diagnostic consumables locally, cheap, and reliably. These diagnostic consumables comprise pipette tips, swabs, spin columns, 1.5 ml tubes, and 0.2 ml tubes. Our solution entails strict medical regulations such as cleanroom conditions.[1]

# 2. Evaluation of Approaches

Initially, we created a long list of possible solutions based on extensive research. We shortlisted the list based on the requirements as well as in close exchange with industry experts. Lastly, we ranked the resulting shortlist solutions by production volume and setup cost from 1 (best) to 4 (worst). The result yields that 3D printing is the most feasible solution given the volume and cost target.

## 2.1 Partner with Local Suppliers

We have contacted multiple suppliers of diagnostic consumables in Ghana. Based on the criteria *availability* and *delivery speed*, we identified Labmart[2] as the most promising supplier. They reported having all required consumables in their warehouse in large quantities except spin columns. They can deliver to all locations within Ghana in 3 days or less. As they do not produce the consumables themselves, Labmart is dependent on the supply of the international market. As a result, our proposed solution cannot rely solely on Labmart.

## 2.2 Extrusion

*Production volume: 1; Setup cost: 3*

In extrusion, the desired form of the product is obtained by pushing plastic through a die. From a financial standpoint, the required machinery and the dies for extrusion are affordable and thanks to its continuous production, it has a very high volume and low cost per product, making it a preeminent solution for the challenge. But since the plastic is continuously pushed through a die, the final product has a fixed cross-section whereas all the diagnostic consumables for the

[1] See a complete list of requirements here: https://docs.google.com/document/d/1wC5GGclJcITvUySQfmzM5s1AWAaFe12ICceojfKlqtk/edit?usp=sharing

[2] https://www.labmartltd.com/about-us/

Corona test have varying cross-section. Thus, extrusion was excluded from the discussed solutions.

## 2.3 Polymer Casting

*Production volume: 4; Setup cost: 1*

In a polymer casting process, the model of the desired shape is submerged into a liquid resin or rubber. Later, the model is removed leaving the negative, namely the mold behind. After the creation of the mold, it is filled with a synthetic resin mixed with a curing agent, which will become the product. Later the product is cured by solidifying it while it is inside of the mold and then it is removed from the mold. Recently, Stereolithography 3D printing has started to be used for producing the master mold, which decreases the labor work for mold production.

Polymer casting has a very low lead cost and cost per product thanks to the cheap materials that are used and no need for any machinery. But the main disadvantage of polymer casting is it's required labor, which makes it impractical in an application that requires high production volume. Even though master molds can be formed from SLA printers, each casted part would still require hands-on labor for post-processing.

## 2.4 Injection Molding

*Production volume: 1; Setup cost: 4*

Injection molding works by injecting molten plastic into a mold. Its capability of producing plastic materials with very high volume and excellent quality makes it the traditional method of producing medical consumables. One of the machines that are used in industry is Arburg Allrounder 520 A which produces 50,000 parts per hour. But its size makes it impossible to be used for a mobile application and its price which is higher than 100,000€ is well above the project's budget.

Further research showed that there are more compact injection molding machines that can be fitted inside a container. They tend to be more affordable than the industry sized ones and they are still able to reach the production volume that is required for this project. BOY XS, displayed in Figure 1, seemed to be the most promising one. Thanks to its 0,77 m² footprint, it can be easily shipped for a mobile lab. To learn more about the compact injection molding machines, an interview with the sales manager of the Dr Boy Spritzgießautomaten, Andreas Scheideler has been conducted. During the interview, Mr Scheideler confirmed that the machine is capable of producing plastic consumables of 10 grams per cycle and it had a cycle time of 1.3 seconds. Additionally, with the so-called cassette tool, the mold can be easily changed in seconds for producing different parts. One of the main drawbacks is that it required a Three-Phase Voltage of 400V with 50Hz. Even though Ghana has an exact setting for industrial electric supply, it would be a problem to find an industrial electric outlet near to a mobile lab. The second drawback was the price being 23,900€ just for the machinery. With the addition of the custom molds and cassette tool, it exceeds well over 35,000€ making it infeasible for the project.


*Figure 1: BOY XS injection molding machine*

## 2.5 3D Printing

*Production volume: 3; Setup cost: 1*

3D printers create three-dimensional parts by adding each layer one by one according to instructions based on a CAD model. While it has always been a good option for creating affordable prototypes without any additional equipment, recently it has started to be used in manufacturing lines. Using a 3D printer for plastic production, there exist three main technologies. The first one is the fused deposition modeling (FDM), in which a thermoplastic filament is melted and extruded with a circular cross-section for creating a layer. While it is the most affordable technology, it lacks the resolution and accuracy compared to the other methods. Selective laser sintering (SLS) is a method where polymer powder, usually nylon, is fused by a laser layer by layer. While it has the advantage of not requiring any support, it can not be used in medical applications. The third method is stereolithography (SLA), which cures a photopolymer resin by a laser. It has the best part quality compared to the other two 3D printing technologies and it has been used in the medical field for the drill guides for dental implants. Because SLA printers have been used in the medical field prior and it has a high part quality, it has been chosen as the production method for the diagnostic consumables for the Corona test. It is planned to tackle the relatively low production volume drawback by using multiple 3D printers at the same time.

# 3. Technical Description

## 3.1 Equipment

### 3.1.1 Devices

- SLA 3D Printer
- 3D Printer Post Processing Station
- Wash Machine
- Cure Machine
- Steam Sterilization Device

### 3.1.2 Resin

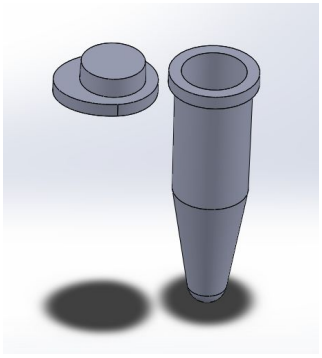
One crucial aspect of the production of diagnostic consumables is the material. There exist plenty of medical and dental resins that are used by practitioners and are well tested. The question is which resin ist the least expensive that also fulfils our criteria. Our research yields that Surgical Guide Resin by Formlabs is the best-in-class resin for our use case.

In a case study by the University of South Florida, Northwell Health, and Formlabs, 3D printed nasal swabs of a 150 mm length with a 70 mm breakpoint using Surgical Guide Resin. They report that it could effectively be sterilized. In a bench lab test they concluded that the swabs can be as effective as the standard polyester swabs in detecting a respiratory syncytial virus. In a clinical trial of 120 patients, no significant difference between the flocked nasopharyngeal swab and the 3D-printed swabs was shown.

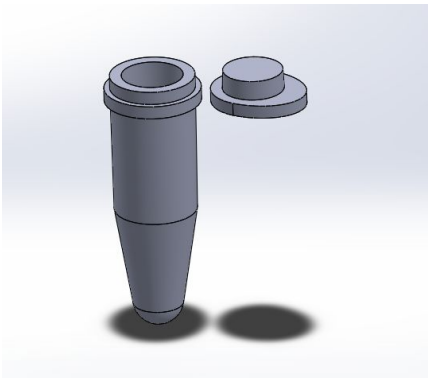
Surgical Guide Resin is a CE certified, biocompatible material that meets Class 1 requirements. The clear resin is designed to print a 100-micron and 50-micron layer line resolution on Formlabs' SLA printer. Surgical guide resin is not cytotoxic (EN ISO 10993-5:2009), non-irritative (ISO 10993-10:2010/(R)2014), and not a sensitizer (ISO 10993-10:2010/(R)2014). It also complies with the requirements for regulatory purposes (EN ISO 13485:2016) and the application of risk management to medical devices (EN ISO 14971:2012). One liter of Surgical Guide Resin costs €225 and is compatible with Form 2, Form 3B, and FOrm 3BL printers. We have also contacted representatives from Formlabs who confirmed that Surgical Guide resin was used in several case studies to produce swabs for real-world use.

BioMed Amber Resin fulfils the same criteria. According to our discussion with Formlabs, the difference to Surgical Guide Resin is that BioMed Amber is marketed towards medical applications as opposed to dental use cases. However, one key characteristic of BioMed Amber resin is its stiffness, which might not be appropriate for swabs.

## 3.2. CAD Models

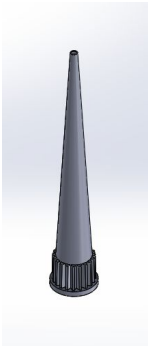


Eppendorf reaction vessel



Spin Column

Swab + Collectiontube



Pipette Tips

After starting to work on CAD design and 3D printing of the plastic consumables, it was quickly realised that traditional designs used in the industry do not work with the 3D printing. The first problem we encountered was the connectors for the caps of the Eppendorf reaction vessel. In the traditional design used in the industry, the cap was connected to the body via a thin connector. This connector part is made of a different material than the one used for the body. It was elastic such that it was possible to move around the cap around the body. It was decided to remove this connector, which simplified the printing and amount of material used.

Another problem that we have encountered during the design was the tightness of the fit for the spin column vessel and container. It was quickly found out that, when the outer radius of the vessel is the same with the inner radius of the container, the fitting is too tight to remove. Hence we updated our design such that the vessel can be now easily removed from the container while making sure that it is tight enough to contain the material inside.

# 3.3. Process

## 3.3.1 Printing

### 3.3.1.1 General Requirements:

- Disinfect the platform used for the batch and all the other materials which might get in contact with the batch with 99% IPA and disposable paper towel.
- The lab technicians have to wear gloves and a face mask when handling sterilized material.
- Gloves and face masks need to be changed if there is an assumption of contamination.
- Otherwise, gloves and face masks should be changed frequently to minimize cross-contamination.

### 3.3.1.2 Organization:

- Each batch needs to be labelled with the name of the printed consumable, the number of consumables, batch number, date of manufacturing, date of packaging.
- Every batch needs to be controlled and the observations have to be registered. (see “Quality Control”)

### 3.3.1.3 Printing Process:

- Upload the PreForm file to the printer.
- Place in the printer the dedicated Tank for the Surgical Guide Resin.
- Select a cartridge of Surgical Guide Resin for printing. Place the cartridge in the printer and open the ventilation valve.
- Insert the previously disinfected Build Platform on the Printer.
- Print the consumables.
- Take the build platform directly to the post-processing station.

## 3.3.2 Washing

- Before handling the printed parts, gloves have to be changed.
- Wash the parts with the Form Wash for 20 min with 99% IPA. (consumables still attached to the build plate)
- Alternatively, the parts can be washed by hand with 99% IPA.
- Allow parts to dry for 30 min
- Control the saturation of IPA using the hydrometer every day (IPA should be changed every 10 batches)

## 3.3.3 Curing

- Change gloves.
- Use sterilized forceps to remove the parts from the platform.

- Place the parts in a support structure for the following curing, the parts shouldn't touch each other.
- Place the support structure with the swabs in the Form Cure to post-cure with the following parameters: 60ºC for 30 minutes.
- Remove the parts from the Form Cure using special sterilized tools.

### 3.3.4 Packaging

- Change gloves.
- Parts are placed in an autoclavable pouch using sterilized forceps.
- The pouch is sealed and the parts shouldn’t overlap.

### 3.3.5 Sterilization

- The packages with plastic consumables are sterilized.
- Pre-vacuum steam sterilizer: 132 °C / 270 °F 4 minutes.
- Alternatively: Gravity displacement: 121 °C / 250 °F 30 minutes.
- The production process is finished; the plastic parts need to be stored in a place away from direct sunlight.

### 3.3.6 Quality Control

After the printing, washing and curing a quality control needs to be carried out.
The parts are checked for printing problems, cracks, distortions or other malfunctions which might be problematic for conducting the Tests with the printed parts.
Defects are registered in a prepared excel sheet with observations and optionally pictures. The parts that don’t fulfill the given criteria are set apart.

# 4. Financial Calculation

The financial calculation estimates the fixed and variable cost for a production of a given number of testing kits (in our example 300). The full calculation can be found here.

Firstly, we assume the following market prices for each consumable and the amount of components required for 300 test kits:

| **Consumable** | **Market price/piece** | **Amount required** |
|---|---|---|
| Swab | €4.50 | 300 |
| Pipette tip | €0.10 | 6,300 |
| Spin column | €1.00 | 300 |
| 1.5ml tube | €0.20 | 1,200 |

| | | |
|---|---|---|
| 0.2ml tube | €0.10 | 600 |

In cell F9, the user can choose between 20 different printers and relevant specifications will be shown automatically (price, build surface, and the resulting component batch size). Surface area, volume per component, and processing time per batch have been hardcoded into the sheet to calculate the total processing time for the test kits.

**First finding:** Exemplarily, we would need 3 Form B printers (7 Anycubic Photon / 1 Form 3BL) to print the required amount of a consumable in one process iteration (except from pipette tips). As we require a high number of pipette tips i.e. 21 parts for one test, the printing time takes disproportionately long compared to the other components.

The subsequent part of the analysis includes a price calculation for washing, curing, sterilizing, and packaging. For this part, we make the following assumptions:

- We require one washing machine with a cost of €500
- We require one curing machine with a cost of €700
- An autoclave is already installed in the mobile lab, so we don't have to add any extra cost for purchase

**Second finding:** The total setup cost considering the purchase of 3 Form B printers (7 Anycubic Photon / 1 Form 3BL) would be at €15,297 (€2,250 / €14,199). The calculation suggests that using 7 Anycubic Photons is more than six times cheaper than using 1 Form 3BL.

Finally, we calculate the variable cost for producing 300 test kits. Based on the total packaging time, we estimate the manual workload to be 11.25h. Furthermore, we assume:

- The cost of a lab worker per hour in Ghana is €1
- The cost of resin per litre is €200
- The post-processing costs 60% of the printing

**Third finding:** We can produce one swab €4.26 cheaper than market price. All the other components are between €0.01 to €0.55 more expensive than market prices. Our analysis shows that only swabs can be produced with a profit while it is more economical to source other parts on the international market. Therefore, other parts should only be printed if the international markets are scarce.

# 5. Outlook and Open Tasks

## 5.1 Prototype evaluation

The prototype showed a good proof of concept. The swabs are flexible enough to take patient samples and the resin is clear enough to see a colour change during the colorimetric test. Furthermore, the resin got even clearer after autoclaving.
The tubes and spin columns were slightly more brittle since they were thicker as the pipette tips and swabs. Consequently, the caps don't always fit perfectly to the tubes and spin column. Additionally, one spin column broke while centrifuging at 13 000 rpm. To solve this drawback a more flexible resin (e.g. Flexible 80A) can be used or the thickness of the CAD Models needs to be decreased.
After autoclaving (125 °C) the prototypes, one 1.5 mL tube showed fine cracks which might also result from the brittleness. Freezing the prototypes at -15 °C did not affect them.
The CAD model of the pipette tip and spin column were slightly off (updated in the new CAD models). The diameter of the spin column was 1 mm too wide. The spin column consists of two tubes and the diameter of the smaller part is the diameter of the actual larger part, therefore both diameters need to be decreased.

## 5.2 Mobile Production Station

The production station needs to be compact, yet the handling of the machines should still be easy. To facilitate production, devices should be removable. When the mobile production station is used for long term usage, more space can be created with additional tables to facilitate the handling of the devices.

## 5.3 Clean Bench

For the packaging of the sterile products, a clean bench is needed. Otherwise, the printed parts could be contaminated after the sterilization.To save money, a clean bench analogue to the one in the Bio.Kitchen could be built. There needs to be enough space for the autoclave.

## 5.4 Packaging Technique

The packaging of the sterilized parts still needs to be elaborated.

## 5.5 Workflow

The final workflow for the production and sterilization needs to be defined. To increase efficiency, a strict schedule with all the different work steps needs to be elaborated. A video can illustrate the different steps.

## 5.6 GIZ Funding

To launch the project, a funding of the “Deutsche Gesellschaft für Internationale Zusammenarbeit” (GIZ) might be useful. Financial support is especially useful for the setup costs of the mobile product station and the know-how is helpful for the cooperation with Ghana.

## 5.7 Logistics

A calendar of the duration of stay in the different laboratories should be managed. The labs need to be contacted far in advance and stay in touch between each other. The logistical and organizational part should be managed by one organization (e.g. Hive Bio Lab).

## 5.8 Certification

To expand the project, a certification for in vitro diagnostic medical devices is needed. Consulting experts can help in this process.