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Additively manufactured nasopharyngeal Swabs for the use in Covid-19 testing

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Abstract: A new methodology to manufacture mucosal membrane contact Covid-19 diagnostic items using powder-bed Additive Manufacturing (AM) and vapor smoothing methods was developed and introduced to fulfill the population testing demand. The technique can rapidly manufacture oral/respiratory diagnostic items at the point of use and at scale. Surface medical device tests were performed to evaluate biocompatibility of such Additively Manufactured Covid-19 diagnostic items. The presented results are the most in-depth medical study of vapor smoothed Additively Manufactured medical articles to date.

I. Introduction

Covid-19 has brought disruption to economic and social life in many countries. Widescale testing of millions of people has been introduced to safely reopen the economy and continuous testing will be needed in the foreseeable future. This has created an unprecedented demand for Covid-19 diagnostics items, among which Nasopharyngeal Swabs are the most widely used.

I.I. New Additive Manufacturing Method

Traditional manufacturing and logistical chains have struggled with sudden spike in demand for Nasopharyngeal Swabs. In fact, re-adjustment of the traditional manufacturing chains for supplying these products proved to be costly, time consuming and energy-intensive process. Additive Manufacturing (AM) has proved to be the quickest and most environmentally friendly approach to ramp up the production and meet the demand. Powder-based AM is able to provide economical solution for the manufacturing of required medical items at scale, especially for specialized Covid-19 Nasopharyngeal Swabs at the required capacity [1]. However, rough, powdery surfaces produced by such method causes the accumulation and growth of bacteria, fungi and increases the risk of the loose polymer particles attacking the respiratory system [2]. Therefore, standard post-processing techniques are not adequate for the smoothing of articles to be used for medical respiratory purposes.

Chemical vapor surface smoothing technology PostPro3D™ by AMT [1,3,4] was found to be the only way to post-process Additively Manufactured PA11 Nasopharyngeal Swabs (AM PA11 NS) manufactured using Multi-Jet Fusion (MJF) powder-based method at scale (Fig. 1). After processing, the surfaces of AM PA11 NS become uniformly sealed, smooth and free of plastic microfibers. To date, around half a million Covid-19 Nasopharyngeal Swabs have been produced using this method [5].

Figure 1: Nasopharyngeal Swabs produced via MJF powder-based method and vapor smoothed with PostPro3D

II. Material and Methods

Biocompatibility test matrix based on ISO 10993-1 and 2016 FDA was used for testing reference [6]. The matrix suggests Nasopharyngeal Swabs require tests for "Limited ≤24 hours Intact Skin Contact" to be performed (Table 1). All test items were solid AM PA11 NS devices with a well defined surface area of 11.23cm^2 each. The study documents and samples were archived according to the OECD GLP for 15 years by TOXI-COOP Zrt. (H-8230 Balatonfured, Galamb u. 12/A). The study was inspected by the Quality Assurance in compliance with the Principles of Good Laboratory Practice.

Table 1: List of conducted tests on PA11 Nasopharyngeal Swabs

Tests conducted	Test method references
Skin Sensitization	ISO 10993-1, 10, 12; EOCD 429
In Vitro Cytotoxicity	ISO 10993-5, 12
Intradermal Reactivity	ISO 10993-10:2013, ISO 10993-1:2012, ISO 10993-1:2018

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III. Results and Discussion

Skin Sensitization results are given in Fig2. No significant (SI ≥ 3) lymphoproliferative responses compared to the relevant negative controls were noted. The observed stimulation index values were 0.8, 0.7 and 0.6 for the 100 %, 50 % and 25 % extracts (respectively) in Extractant 1, while SI values of 1.0, 0.8 and 1.2 were observed for the 100 %, 50 % and 25 % extracts (respectively) in Extractant 2.

According to the OECD 429 evaluation criteria, the lack of the significantly increased lymphoproliferation (SI ≥ 3) up to the maximum surface area/volume of extractant ratio of 3 cm2/mL in the extractants used, as well as the lack of the significant dose-response correlations are considered as evidence that tested AM PA11 NS is not a skin sensitizer.

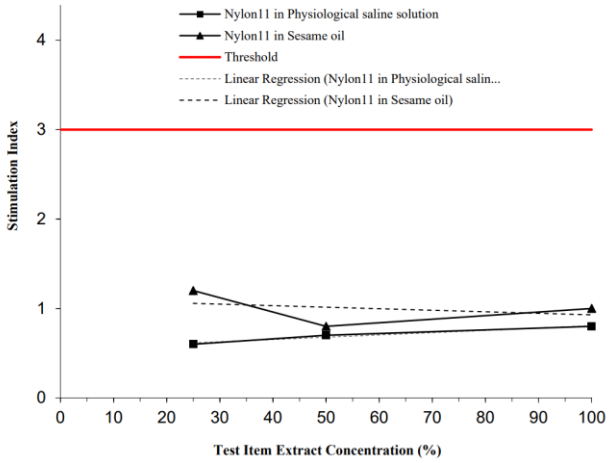

Figure 2: Skin sensitization results

In Vitro Toxicity results for Chinese hamster lung cells are given in Table 2. The test item, vapor smoothed AM PA11 NS did not cause reduction of viability of the cell culture with the highest concentration (100% extract). There was no statistically significant decrease in the number of cell colonies at concentrations of 62.5, 125, 250, 500 and 1000 µL extract/mL. Because the reduction of viability of the cell culture with the highest concentration (100% extract) of the sample extract was less than 30% (0-1%) the test item is considered non-cytotoxic material.

Table 2: In Vitro Toxicity results

Test group	Dose µL extract /ml	Relative survival, %
Negative	-	100
Vapor smoothed AM PA11 NS	62.5	99
	125	100
	250	99
	500	100
	100	99

For Intradermal reactivity test and control items were applied intradermally to the hairless skin of rabbits with 5-5 injections of a 0.2mL dose of test item extracts (polar and non-polar extracts) and 5-5 injections of a 0.2mL polar and non-polar solvent control. Examinations were done immediately after dosing and 24, 48 and 72 hours after the dosing. The overall mean scores are given in Table 3.

Table 3: Intradermal reactivity results

Test	Mean score
Injections of polar extract	0.00
Injections of polar solvent control	0.00
Injections of non-polar extract	0.00
Injections of non-polar solvent control	0.00

Based on 24-, 48- and 72-hours observation time points, the test item AM PA11 NS in polar and non-polar extract form was not irritant. There was no difference between polar and non-polar extract form of the test item. Therefore, the test item AM PA11 NS in polar and non-polar extract form was not irritant.

IV. Conclusions

New AM and vapor post-processing method produces fully compliant Nasopharyngeal Swabs for the use in Covid-19 testing according to ISO 10993-1 and 2016 FDA guidelines. Demand for Nasopharyngeal Swabs is projected to increase supported by periodic testing requirements and high awareness levels of population. Additive Manufacturing offers rapid yet sustainable method to produce these diagnostic items at scale and at the point of use. The gathered biocompatibility data for AM PA11 is the most extensive of its kind to date and enables further use of surface medical device articles for Limited (≤24 hours) mucosal membrane contact. The results also provide positive backing for further possible testing for Prolonged and Long Term contact medical devices if required.

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Author's Statement

Conflict of interest: Authors state no conflict of interest. Informed consent: Informed consent has been obtained from all individuals included in this study. Ethical approval: The research related to human use complies with all the relevant national regulations, institutional policies and was performed in accordance with the tenets of the Helsinki Declaration, and has been approved by the authors' institutional review board or equivalent committee.

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