RETROSPECTIVE STUDY OVER 6 YEARS OF THE TREND IN FUNGAL CONTAMINATION OF CONTROLLED ATMOSPHERE AREAS WITHIN A CELL THERAPY UNIT

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Introduction

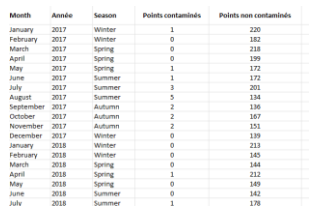
Moulds are aerobic eukaryotic organisms naturally present in the environment. According to pharmaceutics regulations (GMP good manufacturing Practice) , no mould should be present in a controlled- atmosphere zone (ZAC). The seasonal trend in mould contamination of outdoor air is well known, but few articles deal with the trend in fungal contamination in ZACs.

✓ **Primary objective :** to determine whether there is a seasonal trend in contamination in ZACs.

✓ **Second Objective :** to determine the most frequent germs and the effect of factors such as air conditioning, hygrometry and temperature on fungal contamination in ZACs.

Methods

Extraction of Microbiological surveillance data (6 years 2017-2022) from 6 ZACs dedicated to MTI and PTC activities (4 class B and 2 class C)



Month	Année	Season	Points contaminés	Points non contaminés
January	2017	Winter	1	220
February	2017	Winter	0	182
March	2017	Spring	0	218
April	2017	Spring	0	199
May	2017	Spring	1	172
June	2017	Summer	1	172
July	2017	Summer	3	201
August	2017	Summer	5	134
September	2017	Autumn	2	136
October	2017	Autumn	2	167
November	2017	Autumn	2	151
December	2017	Winter	0	139
January	2018	Winter	0	213
February	2018	Winter	0	145
March	2018	Spring	0	144
April	2018	Spring	1	212
May	2018	Spring	0	149
June	2018	Summer	0	142
July	2018	Summer	1	178

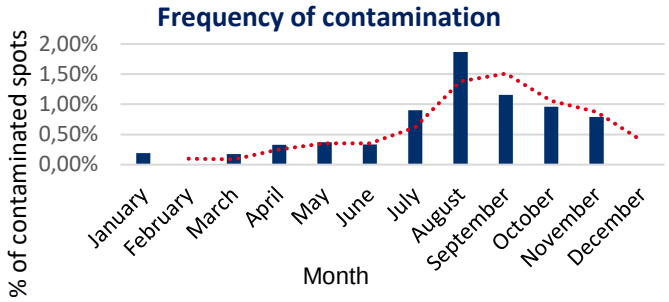
Data collection and management double checked

Statistic test.

Descriptive statistics and hypothesis testing (Kruskal-Wallis test, Dun's test, principal component analysis (PCA))

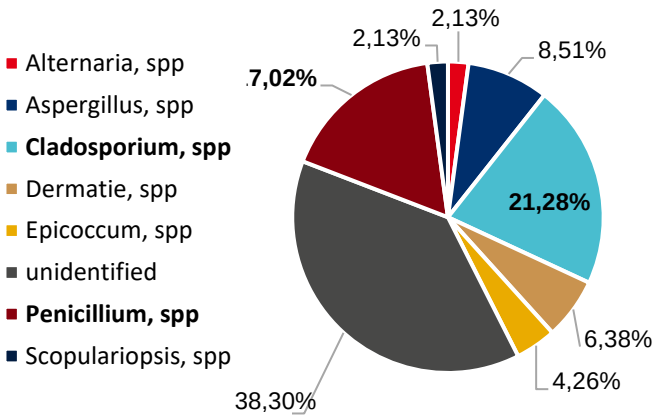
Results

Frequency of contamination

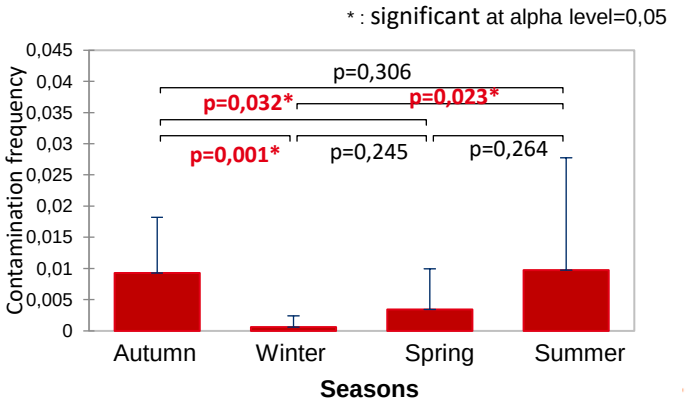


- Contamination peak : **August**
- **December and February** : least affected by fungal contamination
- No difference in fungal contamination between the different months of the year (p-value: 0.070).

Diagram of contaminating fungal species

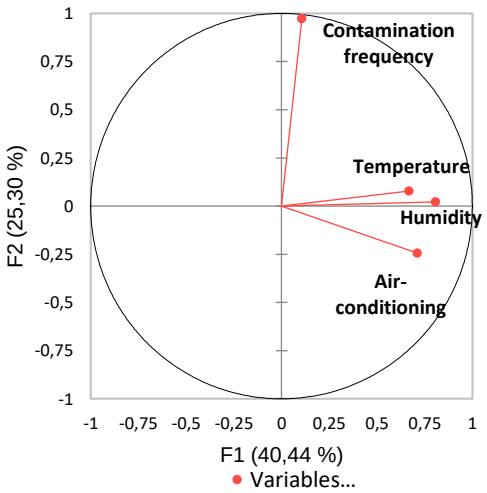


Averages & Standard deviation



- Significant difference in fungal contamination **depending on the season, (p=0.008)**
- Season with the **highest risk of fungal contamination is autumn** and the season with the **lowest risk of contamination is winter (Dun test).**

Principal component analysis



- **The increase in temperature and humidity in ZAC is positively correlated** with the increase of fungal contamination.

Conclusion and discussion

- **Fungal contamination** in our cleanrooms is increased during **summer and autumn**, coherent with the literature : mould spores peaks in environment during summer-autumn period in Europe. It reflects the seasonal evolution of fungal germs outdoors with **Cladosporium** and **Penicillium** being the **biggest impactful species** .
- Favorable **temperature** (24°C and 30°C) and **hygrometry** (from 60 to 65%) are considered main factors.
- Main source of contamination in our cleanrooms would be the biocontamination of entering elements (personnel, materials and consumables), requiring the implementation of **preventive measures** :
  - ➢ adding the **seasonal factor to risk analyses** for microbiological monitoring of cleanrooms, reinforced cleaning with sporicidal, employee awareness.

Reference

- Avis de l'Anses Rapports d'expertises collectives.pdf.
- Basilico M de la LZ, Chiericatti C, Aringoli EE, Althaus RL, Basilico JC. Influence of environmental factors