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MICROBIAL SOLUTIONS

What is Your Identification Program Really Costing You?

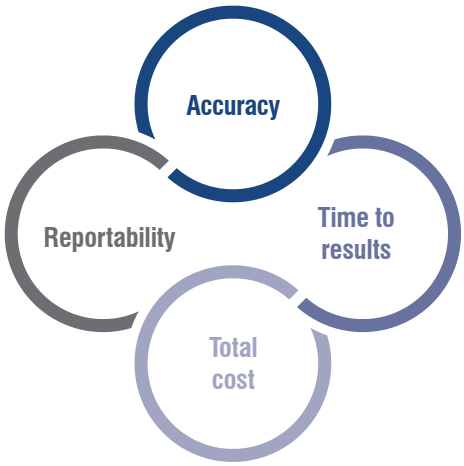
Identification of environmental isolates is a key part of an organization's contamination control strategy. Accurate identifications (IDs) help maintain regulatory compliance, demonstrate a state of control, improve tracking and trending of environmental organisms, facilitate root cause investigations for contamination, and support decision-making. With accurate data, it is possible to fully understand issues that arise and develop an appropriate plan to reduce production recovery time and minimize the impact to the supply chain cycle.

How is a comprehensive cost analysis performed?

Currently, IDs can be made through phenotypic, proteotypic, and genotypic methods. Given the critical aspects of every identification program, it is imperative to select the platform that best fits your needs:

- Eliminates subjectivity
- Provides accurate results
- Assures consistency
- Maintains data integrity

Traditional phenotypic methods differentiate organisms based on their biochemical properties, whereas proteotypic methods identify organisms by their protein spectra generated by matrix-assisted laser desorption/ionization time-of-flight (MALDI-TOF) mass spectrometry. Genotypic methods use comparative sequencing of the ribosomal RNA genes, which is considered the gold standard for the taxonomic classification of bacteria and fungi. Each method and identification platform performs differently in terms of accuracy, reportability, time to results, and total cost.



Each of these areas need to be considered when selecting an identification program, but often only the cost is analyzed. Moreover, the decision needs to be made as to whether identifications will be performed in-house or outsourced. Many organizations assume that performing IDs in-house is less expensive than outsourcing. But are they really?

What needs does your ID program have to address?

In order to assess the true cost of identifications and help compare platforms, organizations should perform a cost analysis that captures all equipment costs, including libraries, service contracts, qualifications, and facilities associated with identifications. The analysis should also evaluate the required labor and time to results. The platform performance parameters should also be considered, and the numbers should be based on the anticipated number of samples being identified per month.

Considerations:

- How can you effectively manage decision making with constant variability in turnaround time of results?
- Is your lab analysts' workload too heavy and impacting lab efficiencies to perform other analysis?
- What is the impact if your preliminary results vary from your final report?

Data-driven cost analysis

Here we share the internal cost analysis performed by a global organization to compare their current identification methods against Charles River's Accugenix® services. The company was using an in-house phenotypic system, and outsourced samples that failed to ID internally to a local lab that used MicroSEQ®. MicroSEQ® is a genotypic identification platform with automated data analysis and a proprietary library.

Charles River's AccuGENX-ID® service consists of comparative DNA sequencing for both bacteria and molds with extensive data analysis using proprietary curated libraries. The AccuPRO-ID® service uses a MALDI-TOF for proteotypic IDs and is backed by DNA sequencing if MALDI-TOF fails to ID the sample.

The data provided in the tables and specific information referencing the data was generated by the organization and has been shared with Charles River.

Table 1: Process steps (in-house labor requirements) to identify isolates by different strategies
This data has not been generated by Charles River, rather an outside organization that performed their own study

	Phenotypic		Proteo/genotypic	Genotypic	Genotypic
	API®	VITEK™ 2	AccuPRO-ID®	AccuGENX-ID®	NCIMB MicroSEQ®
Re-streak isolate	Yes	Yes	No[1]		No[1]
Gram stain	Yes	Yes	No[2]		No[2]
Preliminary tests	Yes	Yes	No		No
Setup assay in-house	Yes	Yes	No		No
Read results in-house	Manual	Automatic	No		No
Post and packaging	No	No	Yes		Yes
Input into in-house trending database	Manual	Manual	Automated Tracking and Trending software		Manual
Labor/TAT	3 days[4]	2 days[4]	TAT: 2 days after receipt of sample for final report[5]		TAT: Preliminary ID 3 days (~3 weeks for final report)[6]
Equipment capacity (no. isolates per run)	n/a	15	n/a		n/a
Number of test sessions per month (~80 isolates)	4-5 (+fungal)	5 (+fungal)	n/a		n/a

[1] It is possible to send the original plate without re-streaking if no other work is necessary on the isolate.

[2] Gram stain is not necessary; however microscopy may be used to distinguish yeast from bacteria.

[3] Can be exported to spreadsheet to combine with in-house data for continuous/complete trending.

[4] This is the total labor not the TAT; the TAT is dependent on resources available to complete work consecutively, and currently the subculture often needs to be repeated due to workload delaying completion of the subsequent tests (this additional work has not been included in these total labor time/cost calculations).

[5] Differential pricing for speed and volume; the calculations in this comparison are based on the quote for 2 day TAT for 80 isolates per month.

[6] The final report is received after 3 weeks regardless of the differential pricing for faster preliminary results, which is sent by email and can differ from the final report; no action can be taken on the result until the final report is received.

Considerations:

- Are phenotypic methods worth subjective, inaccurate results that still cost money?
- What dollar value can you place on decreasing repeatability and increasing confidence, accuracy, and efficiency with outsourcing?

Risks associated with phenotypic and other in-house methods

First, for the internal cost analysis, the in-house labor requirements were analyzed (Table 1). Phenotypic methods require additional processing steps like re-streaking for isolation and Gram stains before identifications can be made. There is an increased risk of human error with increased handling of the sample. The preliminary in-house tests require critical training of staff due to the multiple and complex decision points that can depend on subjective data. A fully capable testing lab must also maintain and manage validated and qualified inventory, such as reagents, consumables, and equipment to perform identification test methods and growth promotion studies. The turnaround time (TAT) until identification reports are received varies from 2 days to 3 weeks, with varying amounts of labor required for interpreting and recording the identification results. Also, the risks to data integrity should be acknowledged for manually reading results and recording them in the in-house trending database.

Once the labor requirements are evaluated for in-house versus outsourced identifications, the cost of that labor can be incorporated in the total cost analysis. This includes the capital cost of the instrument, service contracts, validations, trainings, facilities, and reagents and consumables. This total cost is divided by the anticipated number of identifications per year. For outsourced samples, the total cost is the price of the identification plus shipping and handling, and the labor associated with sending out samples. Table 2 below provides a summary of the total costs. It does not include, however, the performance of the platform and cost of retests. Overall, Accugenix® services result in an insignificant cost increase relative to increased accuracy and improved performance, resource allocation, and risk management compared to an in-house alternative.

Table 2: Cost comparison of different identification strategies

	Phenotypic		Proteo/genotypic	Genotypic	Genotypic
	API®	VITEK™ 2	AccuPRO-ID®	AccuGENX-ID®	NCIMB MicroSEQ®
Total cost for single isolate[7]	$178	$170	$178	$248	$402
Total cost per month based on ~80 isolates[8]	$9,542	$9,682	$10,047	$15,158	$27,292

[7] Takes into account all labor, materials, post and packaging, etc.

[8] Takes into account economy of scale.

Accuracy, reportability, and library coverage considerations

As previously mentioned, accuracy, reportability, and library coverage are important factors that should also be heavily considered in addition to the total cost of an identification strategy. Table 3 summarizes these factors. Does the library of the system offer both broad coverage (number of species) and relevant species (those encountered in production environments as opposed to those from clinical environments) and thus result in an accurate species-level report? There is also a large discrepancy in the capability of these platforms to identify fungal samples, which is of increasing regulatory concern.

Considerations:

- What is the impact of using public databases within a regulated environment?
- How do you justify use of public databases to regulators when using these decreases accuracy and increases the risks of compliance?

Table 3: Performance of different identification strategies

	Phenotypic		Proteo/genotypic	Genotypic	Genotypic
	API®	VITEK™ 2	AccuPRO-ID®	AccuGENX-ID®	NCIMB MicroSEQ®
Technical basis	Morphology and biochemical phenotype		Protein (MALDI) backed up by 16S rDNA sequencing	16S rDNA sequencing	16S rDNA sequencing
Reported accurate results	Medium	Medium	High	High	High
Coverage					
Total number of species in respective databases	No data	426	6,949[9]	> 9,000[9]	1,865[10]
% of in-house bacterial isolate species in the respective databases	No data	67%	100%[9] (MALDI)	100%[9] (16S)	88%[10] (16S)
Ability to identify fungi: Single-celled fungi ('yeast')	*Candida*	*Candida*	Some yeast	Yes (ITS)	Yes (D2)
Mycelial fungi ('mold')	No	No	No	Yes (ITS)	Yes (D2)

[9] A proprietary curated database is used for maximum accuracy.

[10] An uncurated public depository may be used to supplement the database, this may increase coverage % but reduces accuracy and increases the risk of compliance issues.

(16S) the first 500bp of the 16S rDNA is sequenced.

(D2) this method is applicable to Mucorales but unreliable for other fungal species.

(ITS) this method gives species level identification of a wide range of fungi.

Hidden costs of innacurate IDs

One factor not quantified in the analysis is the cost of an inaccurate identification. Methods that yield inaccurate, inconsistent, or no identification are neither useful for tracking isolates to their source nor for generating trend reports. Ultimately, this can lead to a false sense of control, misdirected remediation efforts, additional operational costs, and a threat to brand reputation. Accurate and reliable microbial identification systems are needed:

- For consistent and accurate results to permit tracking of organisms
- For complete investigations
- To avoid delays in product release
- To ensure patient safety

Performing internal cost analysis – let us help you.

The costs captured in this example are specific to this company, the location of their site, and the number of identifications performed. On the other hand, the characteristics in the identification platform performance analysis is inherent to the platform and method. With this consideration, the cost analysis demonstrated that outsourcing identifications can be much more beneficial and cost effective than performing IDs in-house.

If you would like assistance in assessing the true costs of your own identification platform, please contact us.

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