

## ABSTRACT

The fecal marker calprotectin derived from neutrophilic granulocytes is increasingly used in the diagnosis and monitoring of patients suffering from chronic inflammatory bowel diseases. The increasing amount of this analysis is a challenge in the routine laboratory and urgently ask for enhanced automation.

## INTRODUCTION

Fecal Calprotectin (fCP) is a cytoplasmic protein mainly derived from neutrophilic granulocytes. It is considered as a high sensitive inflammation marker.

Calprotectin is well established as an aid in diagnosis of chronic inflammatory bowel disease (IBD) to differentiate between inflammatory and non-inflammatory (e.g. IBS) diseases. As well as for monitoring and therapy follow up of IBD patients.

The Synlab laboratory in Castenedolo is the largest laboratory of the Italian Synlab network; in total it processes about 15 Mio tests per year.

Fecal samples are collected and registered all over Italy and transferred within one day to the main laboratory nearby Brescia where the extraction and analysis were done with manual methods (weighing method/ELISA).

The number of fCP requests has doubled within the last two years and is still increasing. As a consequence the total analysis time has continuously increased.

To solve this unsatisfying situation the lab evaluated and introduced a modern automated assay for fCP quantitation<sup>1-2</sup>.

**What is the impact on the workflow using the BÜHLMANN turbidimetric method.**

## MATERIALS

The BÜHLMANN fCAL<sup>®</sup> turbo can be applied on most clinical chemistry analyzers<sup>3</sup>. At Synlab Italy the method runs on Beckman AU5800 since spring 2017 and replaced the manual ELISA method (Calprest, Eurospital).

To perform a workflow analysis with the two fCP methods we chose the time periods May-Dec2016 (ELISA, n=12'945) and May-Dec2017 (BÜHLMANN fCAL<sup>®</sup> turbo, n=16'538) and we assumed that the total number of customers remained stable.

A comparison between the TAT (total analysis time) from laboratory check-in at Castenedolo to results and from check-in to reports signature was done.

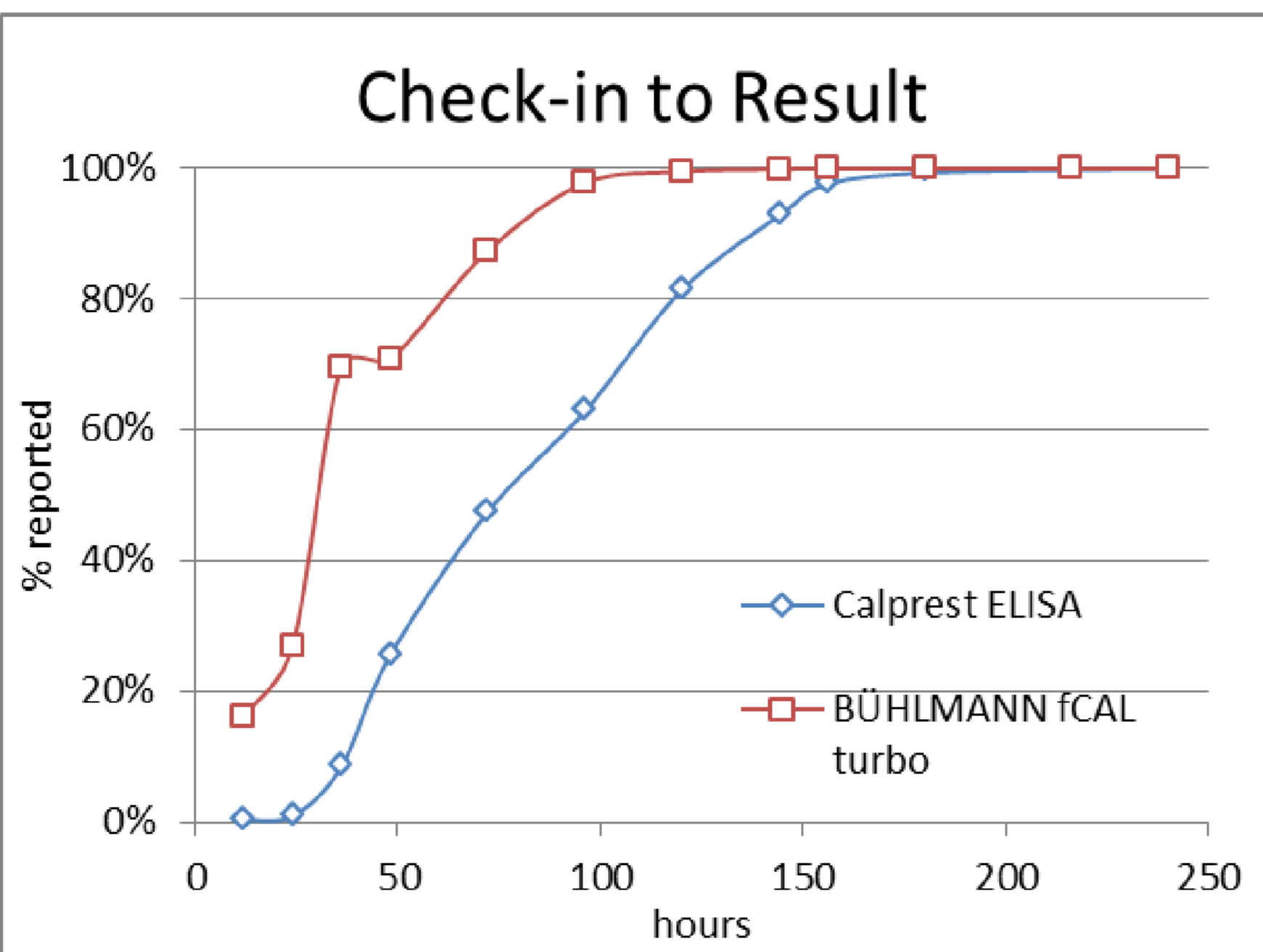
## RESULTS

### Check-in to Result

Calprest ELISA			days	BÜHLMANN fCAL turbo		
hours	#	% reported		hours	#	%
12	24	0.2%	1d	12	2680	16.2%
24	120	0.9%		24	4455	26.9%
36	1089	8.4%		36	11516	69.6%
48	3293	25.4%		48	11698	70.7%
72	6128	47.3%		72	14443	87.3%
96	8127	62.8%		96	16166	97.8%
120	10540	81.4%		120	16464	99.6%
144	12009	92.8%		144	16528	99.9%
156	12642	97.7%		156	16534	100.0%
180	12860	99.3%		180	16536	100.0%
216	12922	99.8%	216	16536	100.0%	
240	12935	99.9%	240	16537	100.0%	

Calprest ELISA		BÜHLMANN fCAL turbo	
1st quartile [h]	47.8	1st quartile [h]	23.7
Median [h]	74.4	Median [h]	29.4
3rd quartile [h]	115.1	3rd quartile [h]	52.3
Maximum [h]	625.3	Maximum [h]	246.8
IQR [h]	67.3	IQR [h]	28.6



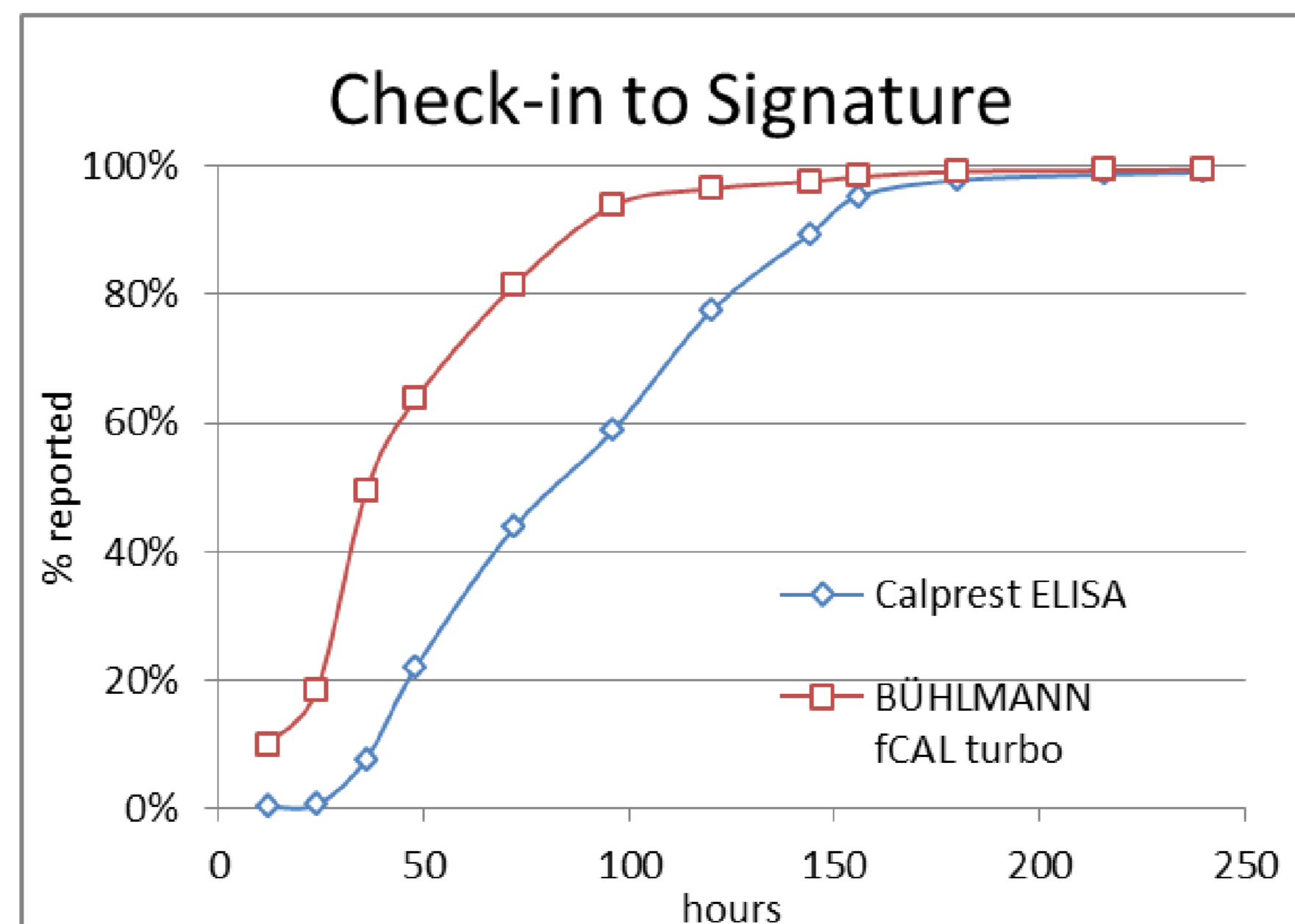
The fCAL turbo method allowed a daily fCP routine activity in our lab. With the manual ELISA method the median time to result was 74.4 hours and 75% (3<sup>rd</sup> Quartile) of all requests were completed after 115.1 hours. With the turbidimetric test a significant reduction was achieved. With the median of 29.4 hours (3<sup>rd</sup> quartile of 52.3 h).

### Check-in to Signature

Calprest ELISA			days	BÜHLMANN fCAL turbo		
hours	#	% reported		hours	#	%
12	16	0.1%	1d	12 h	1620	9.8%
24	74	0.6%		24 h	3050	18.4%
36	987	7.6%		36 h	8159	49.3%
48	2827	21.8%		48 h	10532	63.7%
72	5660	43.7%		72 h	13475	81.5%
96	7607	58.8%		96 h	15513	93.8%
120	10029	77.5%		120 h	15958	96.5%
144	11574	89.4%		144 h	16144	97.6%
156	12341	95.3%		156 h	16266	98.4%
180	12662	97.8%		180 h	16393	99.1%
216	12774	98.7%	216 h	16426	99.3%	
240	12819	99.0%	240 h	16444	99.4%	

Calprest ELISA		BÜHLMANN fCAL turbo	
1st quartile [h]	50.0	1st quartile [h]	26.0
Median [h]	86.3	Median [h]	36.4
3rd quartile [h]	118.2	3rd quartile [h]	59.6
Maximum [h]	1322.3	Maximum [h]	745.1
IQR [h]	68.2	IQR [h]	33.6



Consequently, the time to signature/report was significantly reduced from 86.3 hours (median ELISA) to 36.4 hours (median fCAL turbo).

The indicated TAT includes the transportation time to Castene-

dolo where the fCP method is centralized for the whole country. Transportation varies from a few hours to about 12 hours for the patients living in south Italy.

## DISCUSSION

- The evaluated method allowed a better management of calprotectin testing and a smaller TAT, due to a shorter workflow.
- The method is now running on a big clinical chemistry high performance analyser, able to perform a huge amount of routine tests by not specifically dedicated Personnel, but able to run the main part of the clinical chemistry ones.
- This method allowed the daily measurement of the fCP with shortening of the times from the check-in to the results up to the signature of the reports, thanks to its improvement.
- The concern that fecal material could damage the hydraulic components of the instrumentation was unfounded. It was only necessary to have a greater number of instrumental washes without a particular increase in work for the technicians.
- Fecal specimen collection systems, with automatic extraction, instead of manual, results in shorter processing times.

## CONCLUSION

The fCAL turbo is a highly accurate and clinically proven method.

The introduction of the turbidimetric method on a high throughput analyzer allowed the daily measurement and a 2.5 times (median) faster closing of our requests.

Fecal sample extracts on clinical chemistry analysers is new. Since introduction we didn't observe any significant problems for the instruments or difficulties for the technicians involved.

The introduction of a quantitative extraction device could further streamline the work flow in the laboratory and circumvent the laborious and time consuming extraction itself leading to additional significant reduction of the TAT.

Decentralized sample extraction in a dedicated device would be the final step in fCP simplification and automation.

## REFERENCES

1. Nilson et al.: A novel turbidimetric immunoassay for fecal calprotectin optimized for routine chemistry analyzers. J Clin Lab Anal 2016; 1-6
2. Noebauer et al.: Analytical evaluation of a fully automated immunoassay for faecal calprotectin in a paediatric setting. Biochem Med (Zagreb) 2017; 27(3)
3. Instruction for use BÜHLMANN fCAL<sup>®</sup> turbo assay. BÜHLMANN Laboratories AG, Switzerland