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# Comparison of AI-assisted and manual zone interpretation of Nitroxoline in uncomplicated urinary tract infections

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## Background

Nitroxoline is one of the recommended first-line drugs for the treatment of uncomplicated urinary tract infections (uUTIs). Nevertheless, Nitroxoline is not included in the usual panels of automated susceptibility testing platform systems, such as MicroScan or Vitek. Therefore, manual testing of Nitroxoline using disc diffusion is required in routine diagnostics of urine specimens. With a resulting high number of tests to be interpreted manually, the impact of an automated inhibition measurement is particularly high.

## Methods

- 260 *Escherichia coli* isolates from routine urine samples were tested for susceptibility to Nitroxoline by disc diffusion testing.
- Zone diameters (ZD) were measured and interpreted according to EUCAST breakpoints 2023 (S ≥ 15mm; R < 15mm).
- Each ZD was measured (i) manually by plate in hand as the reference method (ii) by APAS Independence (CCS) AI-Algorithms and (iii) electronically by a microbiologist using the image acquired with the APAS measuring tool (APAS-Human ZD).
- Results were documented in a blinded manner.
- ZD from all three groups were compared according to FDA guidance.
  - Categorical agreement (CA) i.e. no error between test and reference
  - Major error (ME) = R in test instead of S (ii vs. i / iii)
  - Very major error (VME) = S in test instead of R (ii vs. i / iii)

## Results

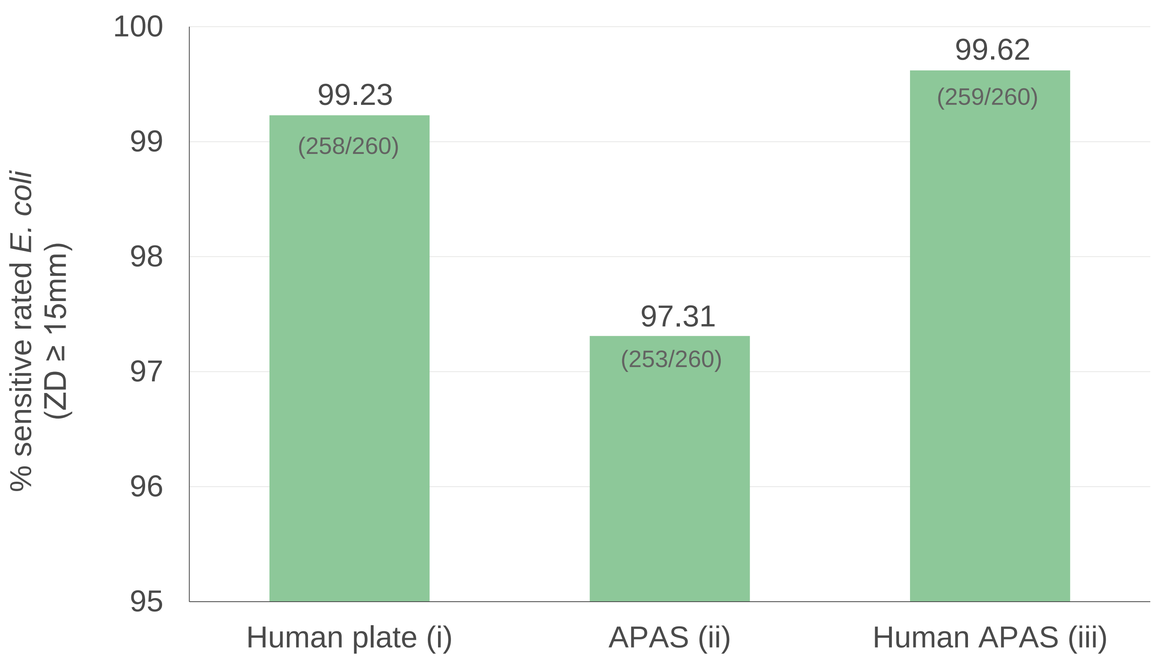


**Figure 1: Rating of susceptibility (S) to Nitroxolin of *E. coli* strains from urinary samples.** APAS rated 97.31% (253/260) of the plates as *E. coli*, sensitive (S, ZD ≥ 15mm) to Nitroxolin. For 253 plates, interpretion was a CA. For 6 plates interpretation was a ME and one plate a VME (see table 1).

## Conclusion

**In this study, we were able to confirm, that Nitroxoline resistance in *E. coli* of urine samples is extremely low with <0.5% (1). We furthermore could show, that the APAS-AMR module has a high categorial agreement (CA) with manual reading of disc diffusion test. The mean value of the zone diameter (ZD) in the three approaches (i; ii; iii) showed comparable results. As no systematic error or difference between human reading and APAS reading was found APAS-AMR is a promising tool for the automated measurement of ZD in the routine microbiological diagnostic.**

## Results

**Table 1 Errors identified by comparing of ZD rating (APAS vs. human).** 6 plates with ME were detected (APAS = R vs. human = S). One plate was rated as VME (APAS = S vs human R). For the plate with the VME, APAS measured the outer circle of the ZD, while human measured the inner circle. See table 2 for manual measured values.

| Human plate in hand (i) | Human rate | APAS (ii) | APAS rate | APAS-Human ZD (iii) | Human rate | Type of Error |
|---|---|---|---|---|---|---|
| 19 | S | 10 | R | 19.7 | S | ME |
| 22 | S | 14.7 | R | 21 | S | ME |
| 24 | S | 11.4 | R | 21.3 | S | ME |
| 25 | S | 11.8 | R | 23.5 | S | ME |
| 30 | S | 11.2 | R | 29.3 | S | ME |
| 23 | S | 10 | R | 23 | S | ME |
| **14** | **R** | **23.2** | **S** | **15.7** | **R** | **VME** |

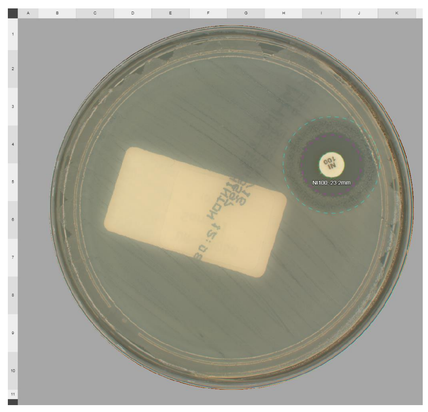

**Figure 2: Isolate with ZD at the breakpoint.** As a VME, ZD was rated by 6 microbiologist (rates see table 2).

**Table 2: Rating of ZD near breakpoint (15mm) by APAS-Human ZD and 6 different microbiologist (M).** Rating by M was 50:50 for sensitive (S) vs resistant (R). APAS flagged the plate with a 'double zone' for review and thus would not release the result.

| Assessor | Measurement [mm] | Susceptibility |
|---|---|---|
| **APAS Human ZD** | **15.7** | **S** |
| M1 | 15.2 | S |
| M2 | 14.7 | R |
| M3 | 15.3 | S |
| M4 | 14.6 | R |
| M5 | 15 | S |
| M6 | 14.7 | R |
| **M Ø** | **14.9** | **R** |

**Table 3: Comparison of ZD measurement means between methods.** No difference could be found in the mean values of zone diameter (ZD) in the three approaches.

| Measurement | Mean ZD |
|---|---|
| Human plate in hand (i) | 24.2 ± 2.1 |
| APAS (ii) | 24.1 ± 2.4 |
| APAS-Human (iii) | 24.8 ± 3.8 |

## References

(1) Jazmati et al., Eurosurveillance, 2022

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