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Title:	Verification of Decision Level and MDA Under ANSI/HPS N13.30-2011
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Verification of Decision Level and MDA Under ANSI/HPS N13.30-2011

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DOELAP for Radiobioassay Webinar

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Disclaimer

- Although very well reasoned, the information and opinions in this presentation are my own and do not represent any official position of DOELAP or Los Alamos National Laboratory.

Introduction

- The 2011 revision to ANSI/HPS N13.30, *Performance Criteria for Radiobioassay* added criteria the periodic evaluation of the decision level (DL) and minimum detectable amount (MDA).
- Some aspects of these criteria raise questions on how they are to be implemented for bioassay measurement systems.
- The intent of this presentation is to summarize some of the issues and initiate thought and discussion on methods to address them and provide consistent evaluation criteria.

Requirements

- ANSI/HPS N13.30-2011 Section 4.4, *"The service laboratory shall periodically assess the MDA, decision level, relative bias, and relative precision."*
- DOE-STD-1112-2016 (2.1), *"ANSI/HPS N13.30-2011 is incorporated into this standard. DOELAP may modifiy any specification as necessary to assure conservatism in the accreditation process."*
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Requirements (cont.)

- Requirements for testing of Lc, MDA/MDC are not completely new:
  - ANSI/HPS N13.30-1996 Section 3.4.4, "*The service laboratory shall periodically assess the MDA, relative bias, and relative precision.*"
  - DOE-STD-1112-98 Checklist (QA 9), *"Quality control protocols are in place and include: … Verification of Lc, MDA, and/or MDC determinations"*
- However, no criteria were provided for verification of these quantities until the 2011 revision.

Verification of Detection Quantities

- Computational checks can be used to validate that algorithms are correctly calculating quantities, but will not test if the assumptions going into those quantities are correct.
- MDA and DL equations presented in 13.30-1996 are generally based on equations presented by Lloyd Currie (1968 and subsequent) and assume parameters are normally distributed.
- For low-level measurements the assumptions inherent in these formulations do not apply resulting in Type-I (False Positive) error rates significantly different than expected (see Strom & MacLellan 2001).

Verification (cont.)

- ANSI/HPS N13.30-2011 presents methods and criteria for empirical testing of DL and MDA.
- Failure of verification measurements may indicate:
  - there are systematic and/or random sources of uncertainty not accounted for in the calculation, and/or
  - the distribution is not normally distributed (e.g., values of $K\alpha$ and $K\beta$ are not appropriate for the distribution).

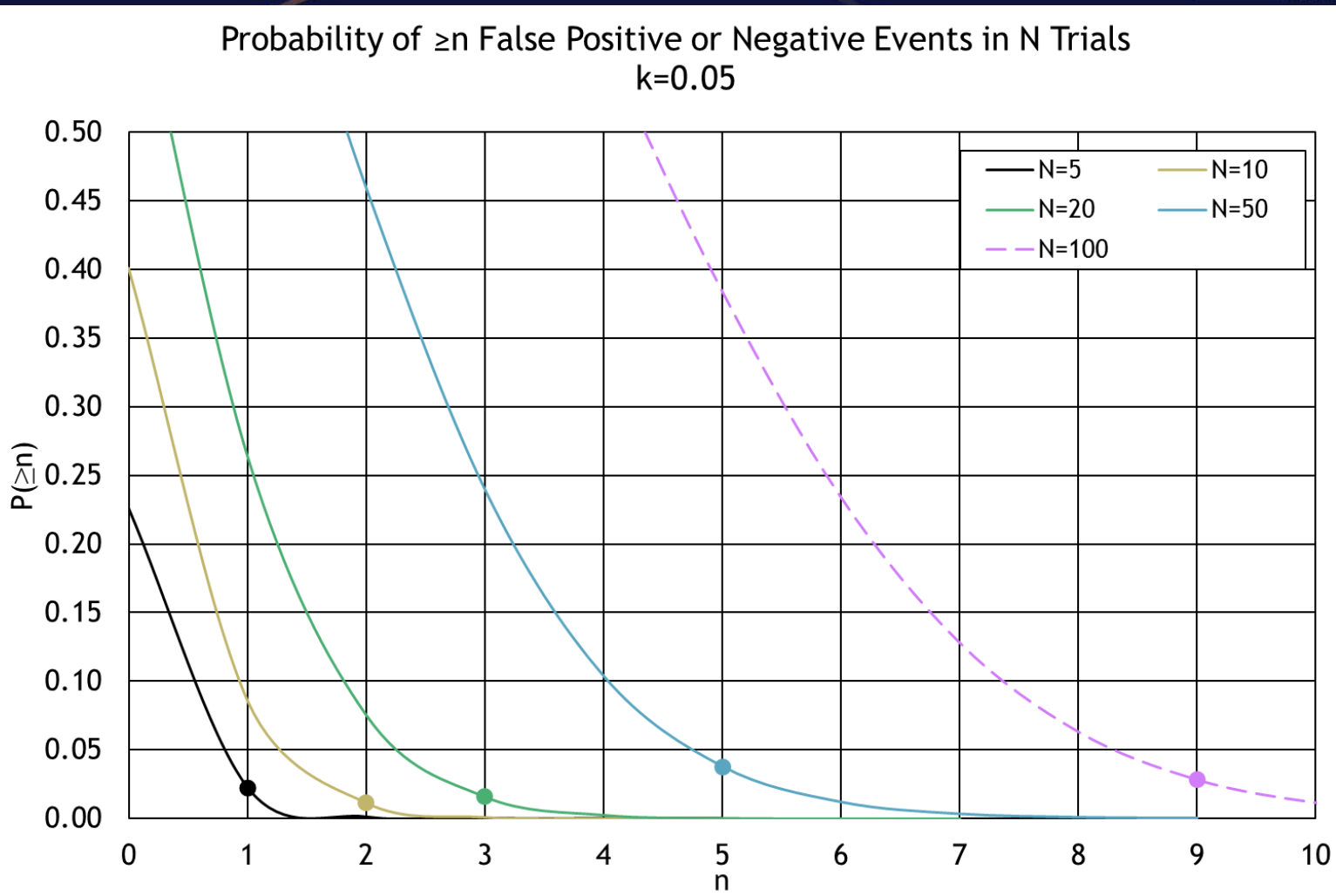
ANSI/HPS N13.30-2011

- Section 4.4 specifies methods and criteria for evaluation of DL and MDA.
- DL is to be verified by "*analyzing identical appropriate blank samples, or by making replicate measurements of an appropriate blank phantom*" and determining number of false positive determinations. (4.4.2)
- MDA is to be verified by "*analyzing identical control samples spiked with an analyte concentration equal to the MDA or making replicate measurements of an appropriate phantom containing such an amount.*" and determining the number of Type-II (false negative) decisions. (4.4.3)

Performance Criteria

The maximum number of incorrect detection decisions is calculated using the binomial distribution. Criteria given 13.30-2011 are based on a 5% significance level. The table below shows the maximum number of acceptable incorrect detection decisions for $K\alpha$ or $K\beta$=0.05.

N Trials	Acceptance Critera
5	1
10	2
20	3
30	4


Probability of ≥n False Positive or Negative Events in N Trials
k=0.05
P(≥n)
0.50
0.45
0.40
0.35
0.30
0.25
0.20
0.15
0.10
0.05
0.00
0
1
2
3
4
5
6
7
8
9
10
n
N=5
N=10
N=20
N=50
N=100

Verification of DL

- Perform replicate counts on appropriate blanks and tally the number of false positives.
- Analyze using routine algorithms and tally the number of false positive results.
- The proportion of false positive results should be less than the confidence level set for the DL (α).
- For indirect bioassay, blanks must have the same physical and chemical characteristics as routine samples, including interferences.
- For direct radiobioassay, “blanks” must replicate the background seen in unexposed individuals (i.e, due to ^{40}K).

Verification of DL (cont.)

- For direct measurements ANSI specifies "*... replicate measurements of an appropriate blank phantom.*"
- Questions:
  - For direct bioassay systems would measurements on unexposed subjects be acceptable?
  - Is the false positive rate to be based on individual nuclides or for all nuclides in an analysis?

Verification of MDA

- Analyze replicate samples/phantoms containing activity at the MDA and tally the number of false negative results.
- For indirect radiobioassay: Spike simulated sample matrix at the desired MDA and process using methods for routine samples. Simply counting an “MDA” sample will only address the counting uncertainty and not the distribution in radiochemical recovery.

Verification of MDA (cont.)

- Direct radiobioassay: ANSI/HPS N13.30-2011 specifies performing replicate counts on “an appropriate phantom” containing activity corresponding to the MDA.
- This could mean that facility to obtain multiple “MDA” phantoms due to differing MDAs between systems.
- Traceable standards may not be readily available for all nuclides of interest to a radiobioassay program.
- Verification of MDAs for short-lived nuclides would lead to “frequent” replacement of phantoms.

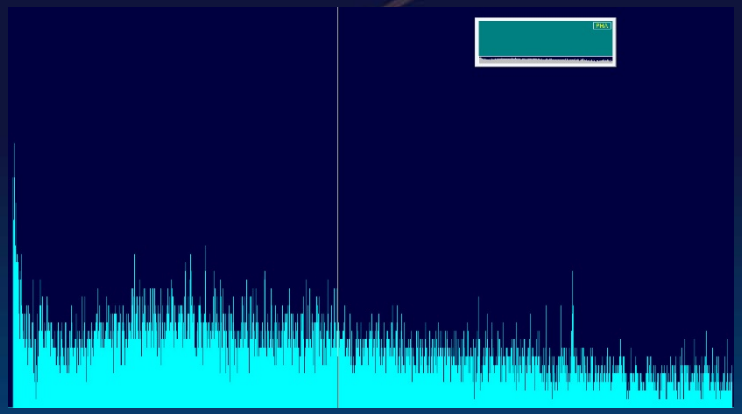
Verification of MDA (cont.)

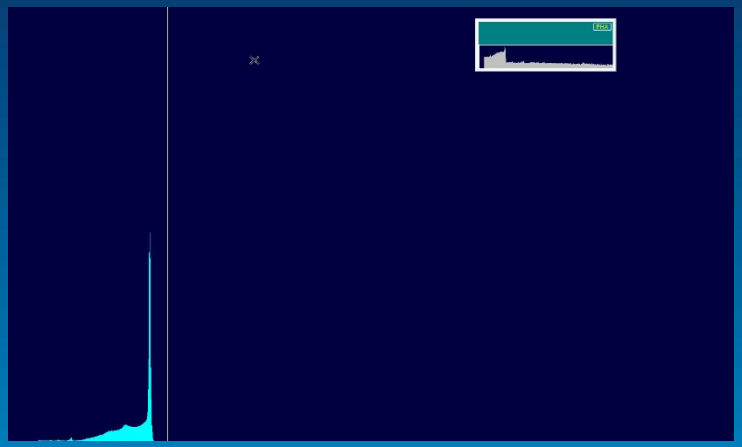
- Questions:
- What MDA values are to be verified? MDA for a system/process or customer required MDAs?
- What nuclide MDAs are required to be verified?
  - All radionuclides of interest in a program?
  - Only those applicable to DOELAP performance testing?
  - Nuclides used for calibrations? ...

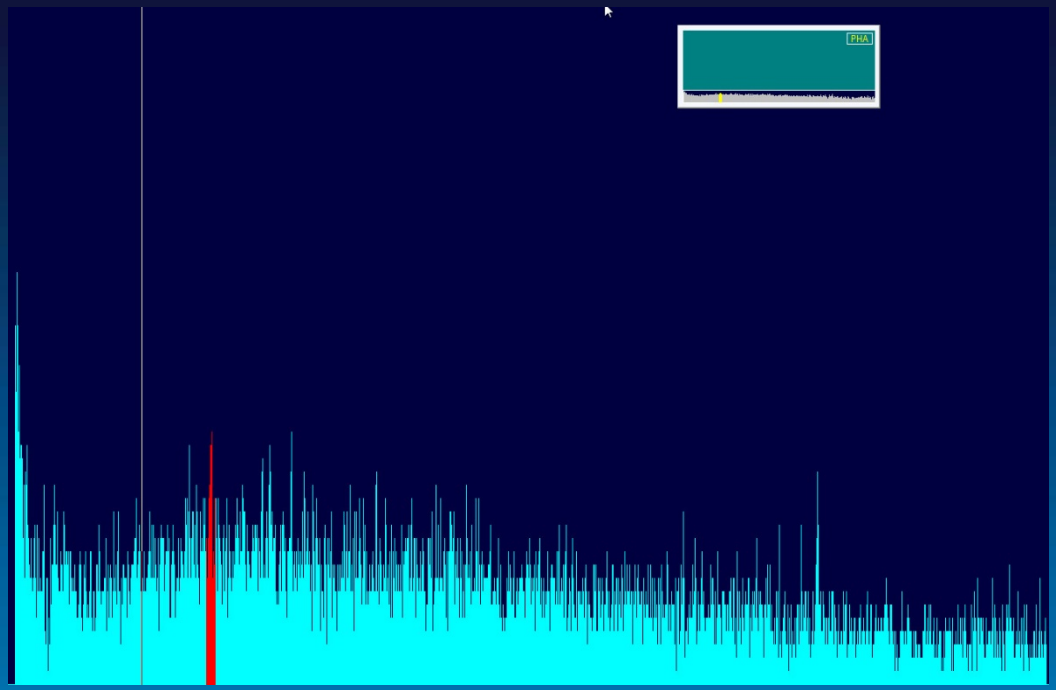
Questions (cont.)

- Are methods other than the use of phantoms acceptable?
  - Simulated spectra?
    - Spectra simulation software
    - Spectrum “summing”
    - Electronic “pulsers” to simulate photopeaks
  - Placement of sources to simulate MDA count rates?

Example of Spectrum Summing







Conclusions:

- ANSI/HPS N13.30-2011 requires periodic evaluation of MDA, DL, relative bias and relative precision.
- DOE-STD-1112-2016 incorporates 13.30-2011 by reference but reserves the ability to modify the requirements.
- If the 13.30-2011 requirements are to be implemented as part of DOELAP a number of issues need to be resolved to provide consistent evaluation criteria:
  - What nuclides need to be verified
  - What is an appropriate frequency of verification
  - Are alternatives to the use of phantoms acceptable
  - …

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Questions & Discussion