MIRION TECHNOLOGIES

Robust, Ready-to-use Radionuclidic Impurity Analysis

Apex-Guard™

Gamma Spectroscopy Application

The Apex-Guard application is an advanced gamma spectroscopy solution designed to meet the stringent demands of regulated count rooms. It provides defensible and ready-to-use impurity calculations and reporting, enabling radioisotope producers to reliably fulfill regulatory requirements such as U.S. FDA 21 CFR Part 11*, and elevate the overall quality of radioisotope production.

The Apex-Guard gamma spectroscopy application builds on Genie™ and Apex-Gamma™ software to provide enhanced controls, security, audit features, and data integrity to support compliance and quality needs of regulated count rooms.

Defensible, Ready-to-Use Impurity Analysis

Radioisotope producers for radiopharmaceutical applications routinely perform quality assurance measurements to demonstrate the radionuclidic purity (RNP) of their products. In gamma spectroscopy, this is achieved by evaluating the sample for impurities and demonstrating the impurities are below a percentage of the total sample activity. To accomplish this with reliability and confidence, the Apex-Guard software impurity analysis algorithm* evaluates the activity of any defined impurity radionuclide against the activity of the sample, which can be compared to a user-defined limit.

FEATURES

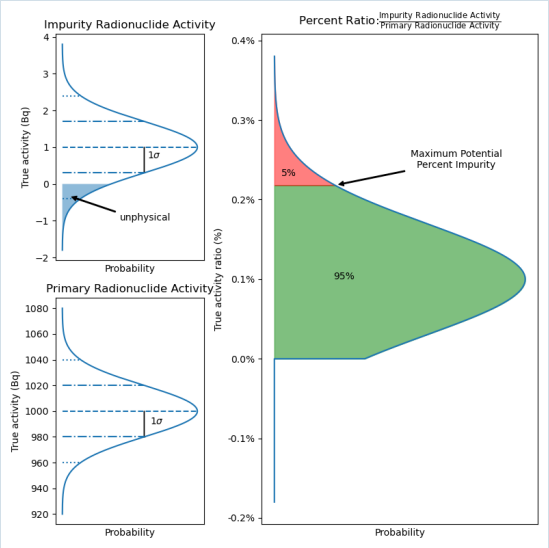
- Streamlined reporting of radionuclidic impurity percentages at multiple reference dates
- Defensible and ready-to-use impurity analysis algorithm*
- Optimized measurement starts and durations with new counting features
- Role-based security with Windows User logons and automatic timed logoffs
- Enhanced security for analysis, device control, and data processing files
- Comprehensive audit logs with change control and auditing capabilities
- Integrated electronic signatures in line with U.S. FDA Title 21 CFR Part 11
- Premium local support options and software updates with subscription service
- Training classes, IQ/OQ services, and startup assistance available

The reference sample activity can be defined in a number of ways, including externally-reported activity or from the same gamma spectroscopy measurement. For both the sample activity and the impurity activity, the Apex-Guard impurity algorithm accounts for measurement uncertainties and introduces a new metric — Maximum Potential Percent Impurity (MPPI) — providing defensible, confident reporting of the sample's radionuclidic impurity.

What Does Apex-Guard Impurity Analysis Provide?

The impurity algorithm divides the probability distribution of the impurity activity by the probability distribution of the sample activity, and then identifies a value that is the highest likely percentage (based on a user-defined confidence) of the true impurity activity to the true total sample activity. This percentage is called the Maximum Potential Percent Impurity, or "MPPI".

This method is effective for both identified and unidentified radionuclide impurities. In cases where no peak is found, the MPPI reflects the sensitivity of measurement setup, preventing false reporting of a radionuclide below the below the configured limit.



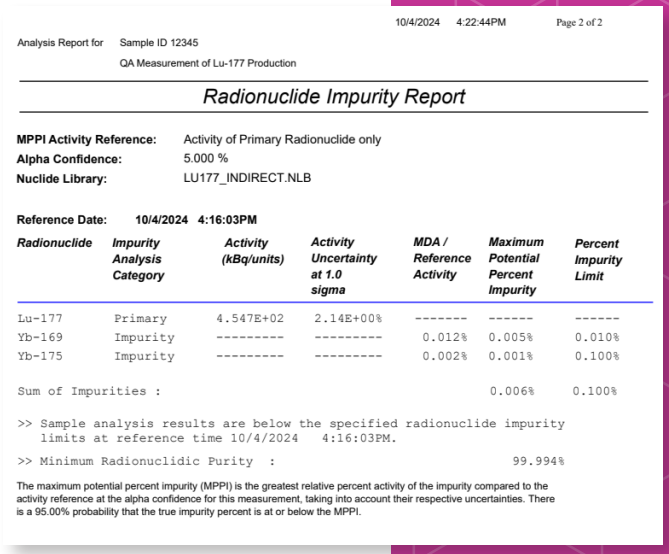
IMPURITY REPORT

The Apex-Guard Impurity Report enables users to set impurity limits for individual radionuclides and for the total impurity activity in the sample. These limits are displayed alongside the MPPI value for each impurity for easy understanding of results. The report displays activity, minimum detectable activity (MDA) divided by reference activity (which could be the total sample activity or the primary radionuclide activity, for example), and MPPI for each radionuclide.

The report makes it easy to assess if results are below the user-defined acceptable limits:

- **All Results Lower than Limits** — If the MPPI is lower than the user-defined limit for all radionuclides, and the sum of MPPI values are lower than the total sample limit, the report will include the statement, “Sample analysis results are below the specified radionuclide impurity limits.”
- **Any Result Higher than Limit** — If any MPPI value is higher than its associated radionuclide limit and/or the sum of MPPI values exceeds the total impurity limit, the line will be highlighted and no analysis evaluation statement is included.

A secondary detail impurity report shows information for each radionuclide emission line, useful for evaluating the spectrum analysis and performing additional investigation, if needed.



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Analysis Report for Sample ID 12345
QA Measurement of Lu-177 Production

Radionuclide Impurity Report

MPPI Activity Reference: Activity of Primary Radionuclide only
Alpha Confidence: 5.000 %
Nuclide Library: LU177_INDIRECT.NLB

Reference Date: 10/4/2024 4:16:03PM

Radionuclide	*Impurity Analysis Category*	*Activity (kBq/units)*	*Activity Uncertainty at 1.0 sigma*	*MDA / Reference Activity*	*Maximum Potential Percent Impurity*	*Percent Impurity Limit*
Lu-177	Primary	4.547E+02	2.14E+00%	-------	------	------
Yb-169	Impurity	---------	---------	0.012%	0.005%	0.010%
Yb-175	Impurity	---------	---------	0.002%	0.001%	0.100%
Sum of Impurities :					0.006%	0.100%

>> Sample analysis results are below the specified radionuclide impurity limits at reference time 10/4/2024 4:16:03PM.

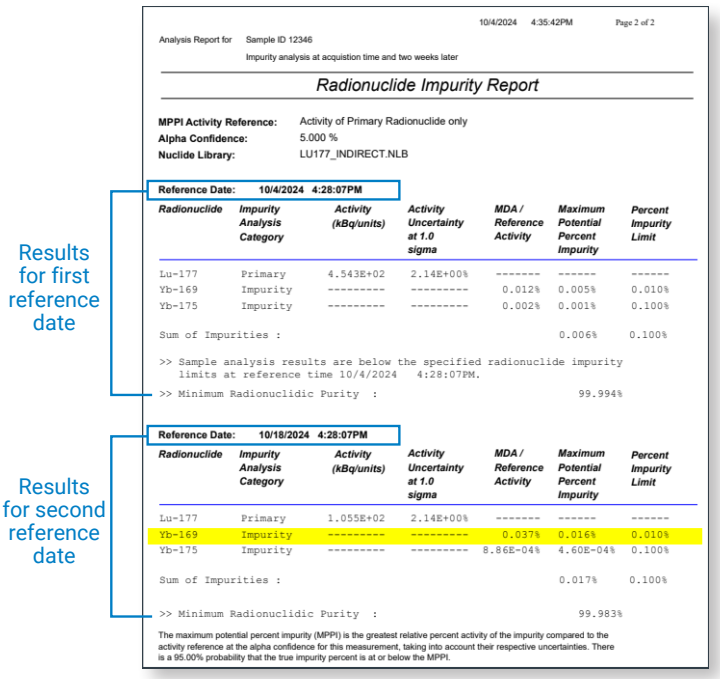
>> Minimum Radionuclidic Purity : 99.994%

The maximum potential percent impurity (MPPI) is the greatest relative percent activity of the impurity compared to the activity reference at the alpha confidence for this measurement, taking into account their respective uncertainties. There is a 95.00% probability that the true impurity percent is at or below the MPPI.

Radionuclide Impurity Report

REDUCE MANUAL WORKFLOWS WITH REPORTING AT DUAL REFERENCE DATES

A convenient, time-saving feature of Apex-Guard reporting is the ability to include results at two reference dates, such as the time of assay and the time of patient injection. These dates are selected during the sample definition step in Apex-Guard, and then the analysis results, including activity and MPPI values, are decay-corrected to both reference dates. The Apex-Guard Impurity Report then presents both sets of results in a single, concise report, with each section clearly labeled with its respective reference date. This eliminates the need for offline or manual decay corrections or generating two separate sets of analysis results for each sample measurement.



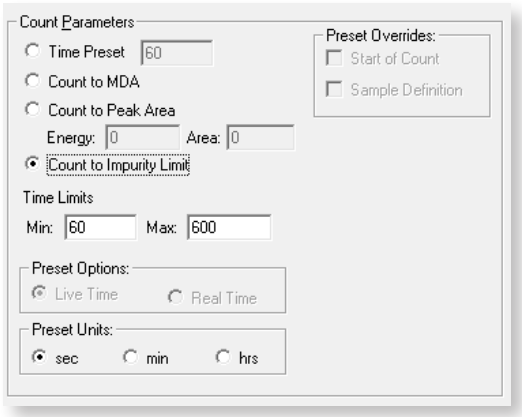
Radionuclide Impurity Report Dual Reference Dates

OPTIMIZE MEASUREMENT WITH FLEXIBLE COUNTING OPTIONS

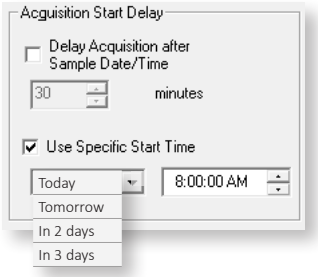
To optimize the amount of count time needed for any measurement, Apex-Guard software supports four counting modes:

- Count to preset live or real time
- Count to MDA
- Count to Peak Area (New)
- Count to Impurity Limit (New)

The "Count to Impurity Limit" references the procedure radionuclide library and the user-defined impurity limits. The software will first count to a minimum count time and then estimate the remaining time required to reach the limit for every impurity. It will continue to re-evaluate the spectrum as the count time continues, stopping only once the MPPI is below the limit for each impurity or the maximum count time is reached. The Count to Impurity Limit feature can also be used to count to the limit defined for the sum of impurity activities.

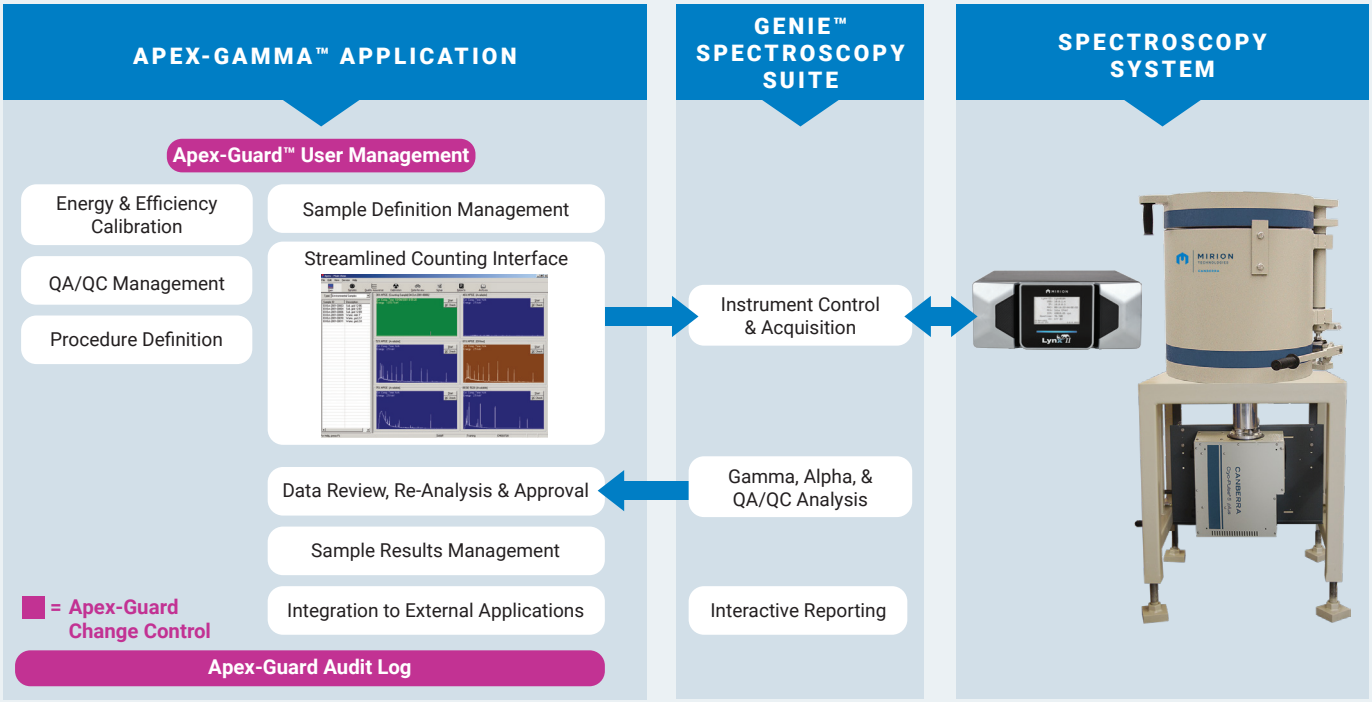


Count Parameters



Acquisition Start Delay

Additionally, Apex-Guard software offers a feature to initiate a count at a specific future time. The acquisition start delay lets users set a specific duration (in minutes) to begin acquisition after the sample is loaded. Alternatively, the "Use Specific Start Time" allows the acquisition to start at a specific clock time. This time can be set for one, two, or three days after the start of the Sample Procedure, extending flexibility to allow short-lived isotopes to decay over a weekend prior to a scheduled acquisition start.



ENHANCED DATA INTEGRITY AND SECURITY FEATURES

The Apex-Guard application builds on Apex-Gamma software to provide extra security, audit log, and data integrity to meet specific compliance needs for the radiopharmaceutical field. These features are also of interest to production counting facilities not under FDA regulation.

The Apex-Gamma Lab Productivity Suite helps laboratories manage gamma spectroscopy operations with features such as sample tracking, calibration management, quality assurance, data review, and reporting. The Apex-Guard application extends the functionality of Apex-Gamma software with these features:

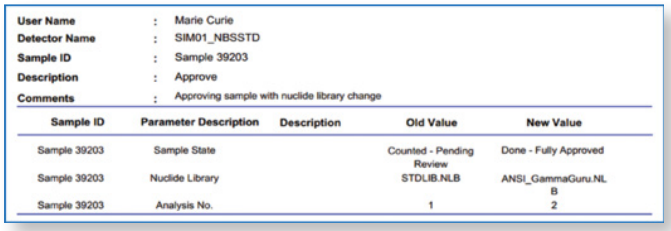
- **Role-based Security with Windows Credentials Authentication:** User profiles are linked to the Windows Login user, which allows Windows Policy settings to manage the password complexity and renewal frequency.
- **Automatic Timed Log-off Feature:** Administrator user setting defines an inactivity time limit and logs the user off the Apex-Guard application when the limit is exceeded.
- **Enhanced Security for Analysis and Data Processing Files:** Editing permissions on essential files for analysis and data are allowed only within the application. This includes calibration, nuclide library, and ISOCS™/LabSOCS™ software associated files (for efficiency calibration and cascade summing correction), QA, and scripts.
- **Enhanced Security on Detector and Multi-Channel Analyzer Controls:** Modification of detector settings configured and active in an Apex-Guard system is restricted outside the Apex-Gamma application, including from Gamma Acquisition and Analysis software. This is now an administrator setting that can be enabled or disabled as needed

CHANGE CONTROL & AUDITING CAPABILITIES

For each change in an application editor, procedure, or QA file, the user is presented with a dialog summarizing the changes during the editing session as well as a text field to record justification for the changes — both of which get saved to the audit log. The text field can be set to optional or mandatory. Another setting enables requesting user credentials and password be entered for authorizing modification.

The enhanced audit log records and displays the following data for a given change:

- Parameter modified
- User who made the modification
- Date/Time stamp of modification
- Value before/after modification
- Justification/comment of modification

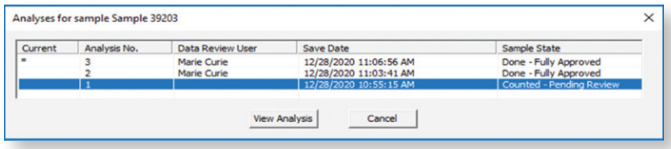


User Name	:	Marie Curie
Detector Name	:	SIM01_NBSSTD
Sample ID	:	Sample 39203
Description	:	Approve
Comments	:	Approving sample with nuclide library change

Sample ID	Parameter Description	Description	Old Value	New Value
Sample 39203	Sample State		Counted - Pending Review	Done - Fully Approved
Sample 39203	Nuclide Library		STDLIB.NLB	ANSI_GammaGuru.NLB
Sample 39203	Analysis No.		1	2

Example Audit Log Entry: Library Modification

Enhanced Data Review: The data review function can display each analysis of a given sample as a separate record, enabling users to view and restore previous analysis settings, including date/time.



Analyses for sample Sample 39203

Current	Analysis No.	Data Review User	Save Date	Sample State
*	3	Marie Curie	12/28/2020 11:06:56 AM	Done - Fully Approved
	2	Marie Curie	12/28/2020 11:03:41 AM	Done - Fully Approved
	1		12/28/2020 10:55:15 AM	Counted - Pending Review

View Analysis | Cancel

Example of analysis records for a given sample

ADDITIONAL FEATURES

- **Electronic Signatures for Signing & Approving Sample Counts:** Signatures include username, function, date/time stamp, and user comments, and conform to the requirements in U.S. FDA 21 CFR Part 11; Electronic Records; Electronic Signatures.
- **Installation Qualification and Operational Qualification (IQ/OQ) Services:** Mirion offers IQ/OQ services, a critical component of GMP compliant solutions. A trained Mirion professional will install the system and review a comprehensive IQ/OQ checklist to satisfy this requirement.*

APEX-GUARD COMPLETE SOLUTION

Apex-Guard software is available as a subscription service, combining priority technical support and software updates. Mirion Services assists in planning, implementing, and optimizing your operations. With the Apex-Guard application, rely on Mirion Services for:

- **Training classes** (offered in person or online) to gain understanding of the options available in the software for your team
- **Installation** of the detector system and Apex application, including collaborating with IT departments as needed
- **Installation Qualification and Operational Qualification (IQ/OQ) service** completed by Mirion Field Service Engineers for required documentation of a correctly installed and operational system, including evaluation of audit log results, user security, and data integrity features.
- **Startup Assistance** builds upon installation and qualification of the Apex-Guard functionality to configure the system for the particular application. This service includes guidance on recommended nuclide libraries, counting geometries, and analysis parameters. For common radioisotopes, Startup Assistance includes documentation of recommendations for independent review and record keeping.

SPECIFICATIONS

For recommended system specifications, including Windows PC requirements, please refer to the Genie 4.0 and Apex® Products Operating System and Database Qualifications resource:

Data storage requirements range from 500 to 3000 assays per 1 GB.

ORDERING INFORMATION

Apex-Guard Software Option

- 1 subscription license required for each computer or virtual machine
- Requires concurrent Genie-Multi and Apex-Gamma license for each computer or virtual machine
- For client/server configurations, Apex-Guard license required for all networked Apex-Gamma computers
- Subscription licenses include updates as released and complimentary technical support

Genie Spectroscopy Suite

- 1 license required for each computer or virtual machine
- Provides acquisition, gamma and alpha analysis, QA/QC, Interactive Peak Fit, and more
- Subscription licenses include updates as released and complimentary technical support

*The Apex-Guard software impurity analysis algorithm is patent-pending. Apex-Guard Software and Mirion's IQ/OQ Service are designed to ensure customers can meet Title 21 CFR Part 11 readily and easily. Please note that Apex-Guard software as a standalone product is not Part 11 compliant and must be integrated with processes and procedures for laboratory Part 11 compliance.

Apex-Guard Software Application

- Gamma Spectroscopy productivity application for operation and management for the production-oriented gamma spectroscopy sample-counting lab
- 1 license required for each computer or virtual machine
- Can be installed as desktop or client/server system
- Requires concurrent Genie-Multi license for each computer or virtual machine
- Subscription licenses include updates as released and complimentary technical support

Installation Qualification & Operational Qualification Services

- IQ/OQ performed by a qualified Mirion support engineer
- Includes co-signed Installation Qualification and Operation Qualification Protocol
- Offered for desktop, client/server, and upgrade systems

Apex-Guard Startup Assistance

- Two-to-three days of consulting expertise available onsite or remotely
- Subject matter expert assistance to configure Apex-Guard counting procedures, nuclide libraries, efficiency calibrations, and analysis parameters to your particular application
- Includes documentation of recommendations to assist in procedure development and external reviews

Apex-Guard Training Classes

- Four-day training course available virtually or onsite for up to 6 students
- Provides overview of Apex-Gamma operations (system setup, counting, procedure configuration, QA management)
- Additional focus on Apex-Guard specific features such as: user accounts and permissions, Apex-Gamma editors and data integrity, change authorization report, audit log, data review and analysis history, digital signatures

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SPC-1-EN-C – 12/2024