Enhanced Quality Product Documentation

Isopropyl beta-D-1-thiogalactopyranoside

PharmaGrade, Manufactured under appropriate controls for use as a raw material in pharma or biopharmaceutical production.

Product Number PHG0010

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Product Regulatory Datasheet - PHG0010

1. General Product Information

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<th>Product Name</th>
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<td>PHG0010</td>
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<td>Qualifier</td>
<td>PharmaGrade, Manufactured under appropriate controls for use as a raw material in pharma or biopharmaceutical production.</td>
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<td>Quality Level</td>
<td>Elite</td>
</tr>
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<td>Sigma-Aldrich Israel, Jerusalem Site, Quality Overview</td>
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<td>IMI TAMI Quality Overview</td>
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</table>

2. Manufacturing, Packaging, Release Site and Supplier Information

Site of manufacturing; IMI TAMI Qiryat Ata, Israel
Site of testing; Sigma-Aldrich Israel Jerusalem Site, 13 Kiryat Mada St. Jerusalem, Israel
Site packaging and product release; Sigma-Aldrich Israel Jerusalem Site, 13 Kiryat Mada St. Jerusalem, Israel
This product is manufactured under appropriate controls to be used in pharma or biopharmaceutical production. This product is manufactured using multi-purpose equipment.

3. Physico-chemical Information

3.1 Synonyms

IPTG
Isopropyl-beta-D-thiogalactoside

3.2 Linear Formula

C₉H₁₈O₅S

3.3 Molecular Formula:

C₉H₁₈O₅S

3.4 Molecular Mass

238.30

3.5 CAS Number

367-93-1

3.6 Origin

The product PHG0010 is manufactured synthetically. According to Sigma-Aldrich Corporation policy, IPTG is considered as animal component free.

Note: The product is manufactured synthetically, via multi-step organic synthesis. The first-stage starting material is of bovine milk origin.

Citing the OIE and the WHO publications, the Official Journal of the European Union in the EC "Note for guidance on minimising the risk of transmitting animal spongiform encephalopathy agents via human and veterinary medicinal products (EMA/410/01 rev.3)" states: "In the light of the current scientific knowledge and irrespective of the geographical origin, bovine milk is unlikely to present any risk of TSE contamination".

The bovine milk is the starting material of the precursor of the lactose used to prepare the first raw material used six (6) steps before isolation of IPTG. In addition, the chemical conditions are extremely drastic and constitute by themselves significant risk mitigation toward TSE.
It is therefore concluded that based on the current regulations (EC) and the chemical synthetic manufacturing process used for preparing IPTG, the related TSE risk is fully mitigated and negligible.

3.7 Manufacturing process
Manufacturing is performed at IMI TAMI. Manufacturing is performed by multi-step organic chemical synthesis including: protection of the carbohydrate (galactose) active groups, followed by further transformational chemical steps; the product is then deprotected and successively crystallized from dioxane and ethanol. Residual dioxane is removed by azeotropic distillation. Galactose used in the first stage is bovine milk origin.

3.8 Specification

<table>
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<th>Analytical Items</th>
<th>Specifications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Appearance</td>
<td>White to off-white powder</td>
</tr>
<tr>
<td>Solubility</td>
<td>Clear, colorless solution at 49.00-51.00 mg/ml water with/without heating</td>
</tr>
<tr>
<td>Water (by Karl Fischer)</td>
<td>NMT 5.00 %</td>
</tr>
<tr>
<td>Elemental analysis (% C anhydrous)</td>
<td>44.86-45.86</td>
</tr>
<tr>
<td>Proton NMR spectrum</td>
<td>Conforms to structure</td>
</tr>
<tr>
<td>Purity (TLC)</td>
<td>NLT 99.0%</td>
</tr>
<tr>
<td>GC (residual dioxane)</td>
<td>NMT 10 ppm</td>
</tr>
<tr>
<td>Specific rotation</td>
<td>-33.0- -30.0 deg at 9.00-11.00 mg/ml water</td>
</tr>
</tbody>
</table>

3.9 Batch results
Certificates of Analysis are available for each lot produced.

4. Regulatory Information

4.1 Compendial compliance
Not applicable.

4.2 Master file
Drug Master File (DMF) is not available for this product.
Certificate of Suitability is not currently available for this product.
Please contact Sigma-Aldrich for further regulatory support.

4.3 BSE/TSE and viral risk statement
This product is not produced using components from animal species (bovine, ovine or caprine) know to harbor BSE/TSE, and is therefore considered negligible risk.
This product is not produced using any bovine, ovine or caprine tissue classified as Category A (per EMEA 410/01 or Specified Risk Material (per USDA 9 CFR 310.22). BSE/TSE risk is negligible.

4.4 Allergen information
This product is not produced with any known major food allergens

4.5 GMO information
The product is not produced using GMOs and is considered GMO free.

4.6 Residual solvents information
The product is produced using class 2-3 solvents: Acetic acid, Acetone and Ethyl alcohol (all class 3) Chloroform, Dioxane, Methanol and Trichloroethylene (all class 2). Acetic anhydride used is not classified.
Final product is analyzed for Dioxane content

4.7 Metal catalyst and metal reagent residues
The product is produced without use of metal catalyst or metal reagent.
4.8 Kosher/Halal status
No status.

4.9 Melamine statement
No melamine contamination risk for this product

5. Miscellaneous Product Information

5.1 Explanation of the lot/batch numbering system
The product is manufactured in a batch process.
Batch size is up to 70 kg
Each produced batch is identified by a specific, unique batch number.
The batch number consists of 8 characters as specified for 054M40XX
- 05 – indicates the month e.g. May
- 4 – indicates the year 2014
- M – indicates the decade e.g. 2010
- 40- indicates production site
- XX – indicates serial number

5.2 Expiration date and/or recommended re-evaluation interval
Recommended retest period is 5 year from QC release.

5.3 Handling, Shipping Conditions and Long-term Storage Recommendation
If stored in the original unopened containers under specified conditions, no significant change of the material can be observed.
- 2 to 8 °C Refrigerator/cooler
- Ship at 2 to 8 °C

5.4 Packaging
Standard pack sizes of 1 g, 5g and 10g.
- 1g packaged in 10 ml amber glass vial
- 5g and 10g packaged in 20 ml amber glass vial
Pack Sizes for larger quantities:
- Glass amber bottles

6. Revision History
Please note that updates are communicated to customers with Change Notification Agreements only.

7. Contact Information
Please contact your local Sigma-Aldrich representative for more information:
SAFC worldwide offices
Sigma-Aldrich Israel Jerusalem Site

Statement 1 - General

Sigma-Aldrich Israel Jerusalem Site is a leading supplier of high quality and purity of biochemical and chemicals for use in molecular biology, diagnostics, cell culture, pharmaceuticals, biopharmaceuticals, life sciences and biotechnology.

1. Facility overview

1.1 Scope
- Sigma-Aldrich Israel Jerusalem Site is located at 13 Kiryat Mada St. Jerusalem Israel.

1.2 Corporate ownership
- Sigma-Aldrich Israel Jerusalem Site facility is a wholly owned subsidiary of the Sigma-Aldrich Corporation, St. Louis, Missouri, USA.

1.3 Customer audit policy
- Sigma-Aldrich Israel, Jerusalem Site welcomes customer audits.

1.4 Site details

General site information:
- 4500 sqm building surface located in 8000 sqm lot
- About 80 employees are working in the building composed of Manufacturing, Research and Development and Support functions. Production operates regularly in one shift of 9 hours, 5 days per week with overtime as required by the process. Equipment is operating 24 hours, 7 days based on process.
- Site activity includes manufacturing and research and development. Several technologies are used to manufacture the different product lines.
  - Fermentation technology providing three product types; cell wall components, proteins (native and recombinant including enzymes), and secondary metabolites (antibiotics like, small molecules). Products could be hazardous and fermentation strain could be risk group 2 for which preventive medicine or interventional medicine exist. Fermentation operation is done Biosafety level 2 large scale and explosion proof segregated areas. All activities as well as waste biological and chemical treatment are done to protect the employees, products and the environment.
  - Multi-step organic synthesis providing different families of organic molecules e.g. carbohydrates, heterocyclic molecules and others.
  - Natural sources extraction and purification providing proteins and enzymes from seeds, plants and animal tissues.
  - Kits, ready-made convenient reagents and protease/phosphatase cocktail inhibitors product line.
- Each manufacturing process includes in-process testing as well as final product QC to conform with internal and customer specifications. Lot specific Certificate of Analysis is available for each lot.
- QC testing capabilities include: melting point, optical rotation, IR, HPLC with UV or ELSD universal detector, UV spectrophotometry, NMR (outsourced analyzed in-house), ICP (outsourced analyzed in-house), TLC, GC, Microanalysis, Moisture determination, Microbiology (i.e. potency), Endotoxin determination, Bioassay/cell based assays, Enzymatic activity with colorimetric and fluorometric detection, N-terminal sequencing (outsourced analyzed in house) Mass spectrometry (outsourced analyzed in-house), Gel Electrophoresis (proteins, nucleic acids), Immunosorbent assay (ELISA).
- Research and development activities including amongst others native and recombinant proteins, fermentation and purification of small organic molecules including semisynthetic molecules and molecules labeling with stable isotopes.
- Primary applications of products: Chemicals and biochemicals used in academic and health related research, pharma, biopharma, and life science disciplines.
- No beta lactam antibiotic is manufactured at the facility. Steroids for research purposes are manufactured at the facility.
- Sigma-Aldrich Israel Jerusalem site monitors processes to ensure conformance to specifications and procedures. Quality inspects all batch lots, adheres to ISO standards in equipment qualification, product testing, method validation, change control, impurity profiles and stability studies. Quality tests and authorizes release of product.
Sigma-Aldrich Israel use approved sub-contractors for cleaning and security services. In special cases for specific manufacturing processes.

2. Compliance Evidence

2.1 ISO registration number and certificates
- ISO 9001:2008, Quality System Register, Inc, Registration No. IQC 18753

2.2 GMP inspections by competent authorities (Regulatory Agencies):
- NA

2.3 Other certifications / registrations
- The site does not have other certification

3. Quality Management Systems Compliance Details

3.1 Quality Management Systems
- General
  Sigma-Aldrich has established a Corporate Quality Policy and Sigma-Aldrich Israel Jerusalem Site facility has a comprehensive Quality Manual.
  - The management system is certified to ISO 9001:2008. Internal audits of the Quality Management Systems are conducted annually to ensure ISO conformance.
  - Responsibilities of Quality Assurance functions include:
    - Management of internal and external audit program
    - Prepare and host customers during customer audits
    - Manage supplier Qualification/Approval status
    - Manage CAPA system and change management system
    - Document and maintain control records associated with manufacturing and quality control
    - Document control related to ISO 9001:2008
    - Document control training activities of new and veteran employees related to quality
    - Disseminate controlled documents to distribution location and archive obsoletes documents
- Documentation
  - Written procedures and approved work instructions are maintained to control documents and data used for the manufacture and verification of products in accordance with ISO 9001:2008 requirements.
  - Quality is responsible for controlled documents and database, which identifies the current revision, effective date and revision history of the document. The database also provides an electronic link to controlled documents.
  - All activities are defined in Standard Operating Procedures, Manufacturing procedures and other supportive documents
  - All documents have a unique identifier, revision number and effective date
  - All activities connected to the manufacturing and testing of the batch and equipment are stored for 10 years from the product release
- Change Control
  - Quality reviews and acknowledges all process variation and deviations. Manufacturing and quality evaluate change requirements prior to manufacturing and/or release to customers.
  - Quality is responsible for change and customer notification. Customer notification on changes is possible provided that a specific agreement is established between Sigma-Aldrich and the customer.

3.2 Management Responsibility
- Management emphasizes the importance of meeting customer needs as well as Statutory and Regulatory requirements
- Verification of Quality System is confirmed through audits
- Management review is conducted annually to review Quality System objectives
3.3 Resource Management
- Management assigns resources and responsibilities where needed to ensure that the quality management system operates efficiently.
- All equipment is subject to written preventive maintenance procedures and qualification programs, if required.
- Work environment is defined and maintained to ensure safe and compliant manufacture of products.

3.4 Product Realization
- Planning: Make to stock based upon First In, First Out (FIFO) or make to order.
- Orders can be placed at www.sigma-aldrich.com, phone, fax, Electronic Data Interchange (EDI) and Business-to-business (B2B).
- Design and Development: New product offer or custom.
- Purchasing via Global Supply Chain capabilities with vendor management per quality, delivery, pricing, and compliance to regulatory requirements.
- Production and Service: Original manufacturer and/or repacker with quality control and quality assurance. Pre and post-sales technical and compliance services. Global distribution capabilities.
- Measuring and Monitoring Devices: Calibration and preventive maintenance.

3.5 Measurement, Analysis and Improvement
- Corrective and Preventive processes – the CAPA process defines steps to review the non-conformance, determine the root cause, evaluate the needs for action to prevent recurrence, implement action, record action and review trends and effectiveness
- Internal Audit are conducted to verify compliance of the quality management system with the ISO9001:2008 requirements
- Nonconforming product controls, electronic, physical segregation, designated areas with signage and within our MRP system
- Continuous Improvement – Key Performance Indicators quality objectives and goals are discussed and realigned at the Management Review meeting.

4. Miscellaneous Site Information
- Sigma-Aldrich is committed to serving the communities where we live and work. We are committed to a safe and fair work environment where our employees can grow and enrich themselves in the diversity that this worldwide organization offers.
- Organization’s responsibility for the environment goes far beyond the specific regions in which they operate.
- By maintaining a solid respect and understanding for our effect on the entire planet, Sigma-Aldrich can provide customers with more-efficient solutions bearing greater benefits, while decreasing material output and environmental impact.
- Batch number has the following structure:
  - First two number designating the month, followed by a one number designated the year, a capital letter designating the decade, two numbers designating the department within Sigma-Aldrich and last two numbers are serial numerical numbers. For example; 034M4824. 03 is March, 4 is the year (in 2014), M is 2010, 48 is the Sigma-Aldrich department and 24 is a numerical serial number
- Environmental controls and monitoring
  - Air. Incoming air is filtered to >95% in all areas. At specific areas such as Biosafety level 2 large scale exhaust air is HEPA filtered. In Explosion proof recovery area exhaust air is carbon filtered. Organic chemistry laboratory has chemical scrubber on air exhaust. Weighing and Packaging department is segregated having HEPA both on air inlet and air exhaust. Air exchange number is according to regulation and activity.
  - Water quality is related to process. Quality could be Double De-ionized reverse osmosis water with or without UV treatment or sterilized tap water. Water quality is monitored
- The Enhanced Quality Program (EQP) is an initiative to provide quality assurance activities that are above what is expected of standard research products. The SAFC EQP provides clearly defined quality traits across a four-level value system: Standard, Premium, Elite and GMP. These tiers reflect various levels of product quality and documentation, according to the application for the product. The Site-Name Facility participates in Standard, Premium and Elite Quality tier products. For more information about EQP, please visit www.safcsupplysolutions.com/eqp.
- Aseptic filling is performed under biological hood
• Sigma-Aldrich Israel Jerusalem Site has redundancy in main equipment to allow proper manufacturing activity and applicable shutdown. Segregated warehouses for raw material and finished goods warehouses exits. A segregated packaging area exist with separate rooms with isolated ventilation, HEPA filters on the inlet and outlet and air handling unit.

5. Contact Information

Please contact your local Sigma-Aldrich representative for more information:
SAFC worldwide offices.
Sigma-Aldrich Israel, Jerusalem Site and Supply Chain Security Overview

1. Scope
   • Sigma-Aldrich Israel, Jerusalem Site. 13 Kiryat Mada St, Jerusalem Israel
   • Corporate ownership: Sigma-Aldrich Israel, Jerusalem Site is a wholly owned subsidiary of Sigma-Aldrich Corporation, 3050 Spruce Street, Saint Louis, MO 63103 USA.

2. Supply Chain Security
   The following controls are executed to ensure the integrity and security of the product in transit from the Sigma-Aldrich Israel to the end user:
   • All packaging/labelling operations are performed on site
   • All products are packed in tamper evident packaging
   • Environmental controls can be implemented during transport.
   • Intermediate storage locations are monitored and reviewed on routine bases. Cold storage units are mapped and revalidated on a two years interval. Full inventory audit occur at least once a year.
   • Only new ISPRM 15 certified plastics pallets are used during shipping

3. Security Information
   3.1 Scope of Security Plan
      • Sigma-Aldrich Israel Security Officer is responsible for the site security
      • Security policy covers site security, physical security and systems as well as emergency response protocols.
      • All new employees are trained according to the security policy and procedures. Yearly training for the security personnel as security officer is performed.
      • Electronic data security is managed under corporate computer usage policy. Data is backed up to remote location on a weekly basis
      • Site access control
        - Perimeter fence secured by sensor system. CCTV coverage of the property. Alarm system connected to central command post. Looks on doors. Panic push button for alarm
        - All doors are controlled by computerized access control system. All employees and subcontractors must wear ID badge. The badge has an RF chip limiting access to areas. All vehicles are registered at ingress/egress. All visitors are accompanied by site employees after identification and registration
   3.2 Personnel Security
      • Each employee receives initial and ongoing training regarding safety, health and environment.
      • Individual employee badges are collected upon permanent leave of the company to avoid unapproved access to the site. Keys are returned upon leaving the company

4. Environmental Health & Safety Program (EHS)
   • Sigma-Aldrich Israel Jerusalem Site EHS mission is to protect our employees, community and environment by complying with all applicable country and local safety, health and environmental regulations and laws
   • The EHS responsibilities include: to maintain zero accident events in our site by continuously training and supervising employees’ safety activity. To maintain zero events of environmental pollution by maintaining strict SOP’s and internal guidance and surveillance. Preparation of site activities for Environmental, Safety and Health internal and external audits. Risk assessment for new or existing activities (machines, chemical or procedures). Implementation and training of existing or new working procedures for Health& Safety activities. Implementation and training of existing or new working procedures for Health & Safety activities.
   • The EHS Department is certified by ISO 9001:2008.
   • The site maintains an Emergency Response Team that is trained on a yearly basis

5. Miscellaneous site Information
   Sigma-Aldrich Israel continuity plan as based on corporate matrix and guidelines
6. **Contact Information**

Please contact your local Sigma-Aldrich representative for more information: [SAFC worldwide offices](mailto:).
CERTIFICATE
NO. 18753

This is to certify that
the Quality Management System of

Sigma – Aldrich Israel Ltd.
13 Kiryat Hamada, Jerusalem, Israel

Was audited by IQC and found to be
in compliance with the requirements of the standard:

ISO 9001:2008

This certificate is valid for
the following scope of activities:

Development & manufacture of bio-chemicals, organic chemicals &
reagents for research, development, production & analytical purposes

This certificate is valid until:

15.06.2017

Date of first approval:

15.06.2005

This certificate is subject to the continuing satisfactory operation
of the Management System and periodic auditing by IQC

22.04.2014
Issue Date

[Signature]
Dan Halpern, President

Institute of Quality & Control Ltd.
6 Ravnitzky St., Petah Tikva 49277, Israel
Tel: 03-9313555, Fax: 03-9044406
E-Mail. info@iqc.co.il, www.iqc.co.il
IMI-TAMI Site

Statement 1 - General

The IMI-TAMI Haifa Site is the Central R&D Institute for Israel Chemicals Ltd (ICL). IMI-TAMI carries out chemical process and product development, from the idea to the final product or process, for ICL. There are fully equipped research laboratories, analytical, corrosion and microbiology/wastewater laboratories, scaleup-pilot facilities and a production job-shop - all on site. In addition, the site is home to the Offices, R&D and Analytical Laboratories of Novetide, a manufacturer of pharmaceutical peptides. This company is jointly owned (50:50) by IMI-TAMI and TEVA Israel.

Facility overview

1.1 Scope
- The IMI-TAMI Site is located at Deshanim Road, Kiriat Ata Industrial Zone, Haifa Israel

1.2 Corporate ownership
- IMI-TAMI is wholly owned by ICL.

1.3 Customer audit policy
- IMI-TAMI welcomes customer audits

1.4 Site details
General site information:
- 10,000 sqm floorspace in buildings located in a 60,000 sqm lot
- About 160 employees (125 from IMI-TAMI and 35 from Novetide) are working on the Site, in research and development, analytical and other support functions and a small-scale production unit operates regularly in one shift of 8 hours, 5 days per week with overtime as required by the process. Equipment can be operated 24 hours, 7 days based on the demand.
- Site activity includes research and development, provision of analytical and test work and small-scale manufacturing. The manufacturing unit has the following capabilities:
  - Multi-step organic synthesis providing different families of organic molecules e.g. carbohydrates, heterocyclic molecules and others.
  - Multi-step inorganic and organometallic processes
  - Extraction and purification of compounds from natural sources – plants and micro-organisms, but not animal tissues.
  - Each manufacturing process includes in-process testing as well as final product QC to conform with internal and customer specifications. Lot specific Certificate of Analysis is available for each lot.
  - QC testing capabilities include: melting point, optical rotation, FTIR, NMR and UV-VIS Spectrometers, HPLCs with UV, Diode Array or Mass Spectrometric detector, GC-MS (incl. Head Space for Volatiles), AA, ICP and ICP-MS, XRD, SEM/EDS, Elemental Analyzer, Karl Fischer and Bioburden analyses. Two Analytical Laboratories – QC-Pharma and Microbiology - are certified GLP for provision of analytical validations, stability studies, assays and 5-batch analyses and biocide efficacy studies.
  - The IMI-TAMI Site monitors processes to ensure conformance to specifications and procedures. Quality Control inspects all batch lots, adheres to ISO standards in equipment qualification, product testing, method validation, change control, impurity profiles and stability studies. Quality Control tests and authorizes release of product
- No beta lactam antibiotic, or steroids, are manufactured at the facility.
- IMI-TAMI uses approved sub-contractors for cleaning and security services.

2. Compliance Evidence

2.1 ISO registration number and certificates
- ISO 9001:2008, Quality System Register, Inc, Registration No. IL-52600
- ISO 14001:2004 Registration No. IL-40475
- OHSAS 18001:2007 Registration No. IL-59444
  ISO certificate can be downloaded from the web-site: http://www.tami-imi.com/certifications
2.2 GMP inspections by competent authorities (Regulatory Agencies):
- NA

2.3 Other certifications / registrations
- The site does not have other certification

3. Quality Management Systems Compliance Details
- The site operates in accordance with current ISO-9001, ISO-14001, OSHAS-18001 guidelines and in accordance with the integrated quality management system requirements.

4. Quality Management Systems
- General
  IMI-TAMI has established a Corporate Quality Policy and IMI-TAMI Site facility has a comprehensive Quality Manual.
  - Internal audits of the Quality Management Systems are conducted annually according to a preapproved audit plan to ensure ISO conformance.
  - Responsibilities of Quality Assurance functions include:
    - Management of internal and external audit program
    - Prepare and host customers during customer audits
    - Manage CAPA system and change management system as per clients requests.
    - Document and maintain control records associated with manufacturing and quality control
    - Document and control training activities of new and veteran employees related to quality
    - Disseminate controlled documents to distribution location and archive obsoletes documents
    - Management training program and calibration program
    - Documentation
      - Written procedures and approved work instructions are maintained to control documents and data used for the manufacture and verification of products in accordance with ISO 9001:2008, ISO-14001, OSHAS-18001 requirements.
      - Quality is responsible for controlled documents and database, which identifies the current revision, effective date and revision history of the document. The database also provides an electronic link to controlled documents.
      - All activities are defined in Standard Operating Procedures, Manufacturing procedures and other supportive documents.
      - All documents have a unique identifier, revision number and effective date.
      - All activities connected to the manufacturing and testing of the batch and equipment are stored for 10 years from the product release
    - Change Control
      - Quality is responsible for changes and for customer notification, if agreed and pre-established between IMI TAMI and the customer.

4.1 Management Responsibility
- Management emphasizes the importance of meeting customer needs as well as Statutory and Regulatory requirements
- Verification of Quality System is confirmed through audits
- Management review is conducted annually to review Quality System objectives

4.2 Resource Management
- Management assigns resources and responsibilities where needed to ensure that the quality management system operates efficiently.
- Equipment is subject to written preventive maintenance as required.
- Work environment is defined and maintained to ensure safe and compliant manufacture of products.
4.3 Product Realization
- Planning: Make to order.
- Orders received by contact the marketing department.
- Design and Development: New product offer or custom.
- Purchasing the purchasing department with vendor management per quality, delivery, pricing, and compliance to regulatory requirements.
- Measuring and Monitoring Devices: Calibration and preventive maintenance, as required.

4.4 Measurement, Analysis and Improvement
- Corrective and Preventive processes – the CAPA process defines steps to review the non-conformance, determine the root cause, evaluate the needs for action to prevent recurrence, implement action, record action and review trends and effectiveness.
- Internal Audit are conducted to verify compliance of the quality management system with the ISO9001, ISO-14001, OSHAS-18001 requirements.
- Continuous Improvement – Key Performance Indicators quality objectives and goals are discussed and realigned at the Management Review meeting.

5. Miscellaneous Site Information
- IMI-TAMI is committed to serving the communities where we live and work. We are committed to a safe and fair work environment where our employees can grow and enrich themselves in the diversity that this worldwide organization offers.
- Organization’s responsibility for the environment goes far beyond the specific regions in which they operate.
- By maintaining a solid respect and understanding for our effect on the entire planet, IMI-TAMI can provide customers with more-efficient solutions bearing greater benefits, while decreasing material output and environmental impact.
- The Batch number system is customized as requested by customer, and should include the production year.
- Environmental controls and monitoring
- Tap water is used through the process. Final crystallization step is performed using De-ionized reverse osmosis water.

IMI-TAMI, Site and Supply Chain Security Overview

1. Scope

2. The IMI-TAMI Haifa Site is the Central R&D Institute for Israel Chemicals Ltd (ICL). IMI-TAMI carries out chemical process and product development, from the idea to the final product or process, for ICL it's located at Kiriat ATA Deshanim road.

   The following controls are executed to ensure the integrity and security of the product in transit from the IMI-TAMI to the customer:
   
   • All packaging/labelling operations are performed on site
   • All products are packed in tamper evident packaging
   • Environmental controls can be implemented during transport according to request
   • Intermediate storage locations can be monitored.

3. Security Information

3.1 Scope of Security Plan

   • IMI-TAMI Security Officer is responsible for the site security
   • Security policy covers site security, physical security and systems as well as emergency response protocols.
   • All new employees are trained according to the security policy and procedures. Yearly training for the security personnel as security officer is performed.
   • Electronic data security is managed under corporate computer usage policy. Data is backed up to remote location on a weekly basis
   • Site access control
     - Perimeter fence surround. CCTV coverage of the property.
     - Most of the doors are controlled by computerized access control system. All subcontractors must wear ID badge. The badge has an RF chip limiting access to areas. All vehicles are registered at ingress/egress. All visitors are accompanied by site employees after identification and registration

3.2 Personnel Security

   • Each employee receives initial and ongoing training regarding safety, health and environment.
   • Individual employee badges are collected upon permanent leave of the company to avoid unapproved access to the site. Keys are returned upon leaving the company

4. Environmental Health & Safety Program (EHS)

   • IMI-TAMI Haifa Site EHS mission is to protect our employees, community and environment by complying with all applicable country and local safety, health and environmental regulations and laws
   • The EHS responsibilities include: to maintain zero accident events in our site by continuously training and supervising employees’ safety activity. To maintain zero events of environmental pollution by maintaining strict SOP’s and internal guidance and surveillance. Preparation of site activities for Environmental, Safety and Health internal and external audits. Risk assessment for new or existing activities (machines, chemical or procedures). Implementation and training of existing or new working procedures for Health & Safety activities. Implementation and training of existing or new working procedures for Health & Safety activities.
   • The EHS Department is certified by ISO 9001:2008.
   • The site maintains an Emergency Response Team that is trained on a yearly basis

5. Miscellaneous site Information

IMI-TAMI continuity plan as based on corporate matrix and guidelines

6. Contact Information

Please contact your local IMI-TAMI representative or Visit us at: http://www.tami-imi.com
Certificate

This is to certify that the Quality Management System of

IMI (TAMI) INSTITUTE FOR RESEARCH AND DEVELOPMENT LTD.
HAIFA BAY

has been audited by SII and found to comply with the Quality Management Standard SI ISO 9001: 2008

scope:

PROVISION OF RESEARCH AND DEVELOPMENT,
PILOT AND LABORATORY SERVICES.
RESEARCH, DEVELOPMENT AND ENGINEERING OF
PROCESSES AND PRODUCTS.

The Certificate is granted in accordance with SII's Rules for the Certification of Quality Systems (AC.04.01 procedure). The validity of the Certificate is subject to the continuous maintenance of the Quality System according to the above standard, and the follow-up surveillance performed by SII. Further clarifications regarding the scope of the certificate and applicability of ISO 9001:2008 requirements may be obtained by consulting the organization.

Date of initial approval: 21.08.2002
Date of expiration: 05.02.2016
License No: 52600
Date of issue: 06.02.2013

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Daniel Goldstein
Director General
Certificate

This is to certify that the
Environmental Management System
of

IMI (TAMI) INSTITUTE FOR RESEARCH AND
DEVELOPMENT LTD.
HAIFA BAY

has been audited by SII and found to comply with the Environmental
Management Standard SI ISO 14001:2004

scope:

PROVISION OF RESEARCH AND DEVELOPMENT,
PILOT AND LABORATORY SERVICES.
RESEARCH, DEVELOPMENT AND ENGINEERING OF
PROCESSES AND PRODUCTS.

The Certificate is granted in accordance with SII's Rules for the Certification of Environmental Management
Systems (AC.04.02.procedure). The validity of the Certificate is subject to the continuous maintenance of the
System according to the above standard, and the follow-up surveillance performed by SII.

Date of initial approval: 11.12.2002
Date of expiration: 05.02.2016
License No: 40475
Date of issue: 06.02.2013

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Certificate

This is to Certify that the Occupational Health and Safety Management System of

IMI (TAMI) INSTITUTE FOR RESEARCH AND DEVELOPMENT LTD.
HAIFA BAY

has been audited by SII and found to comply with the Occupational Health and Safety Management Standard SI OHSAS 18001:2007

scope:

PROVISION OF RESEARCH AND DEVELOPMENT, PILOT AND LABORATORY SERVICES.
RESEARCH, DEVELOPMENT AND ENGINEERING OF PROCESSES AND PRODUCTS.

The Certificate is granted in accordance with SII’s Rules for the Certification of Occupational Health and Safety Management Systems (AC.04.03 procedure). The validity of the Certificate is subject to the continuous maintenance of the System according to the above standard, and the follow-up surveillance performed by SII.

Date of initial approval: 03.02.2008 Date of expiration: 05.02.2016
License No: 59444 Date of issue: 06.02.2013

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