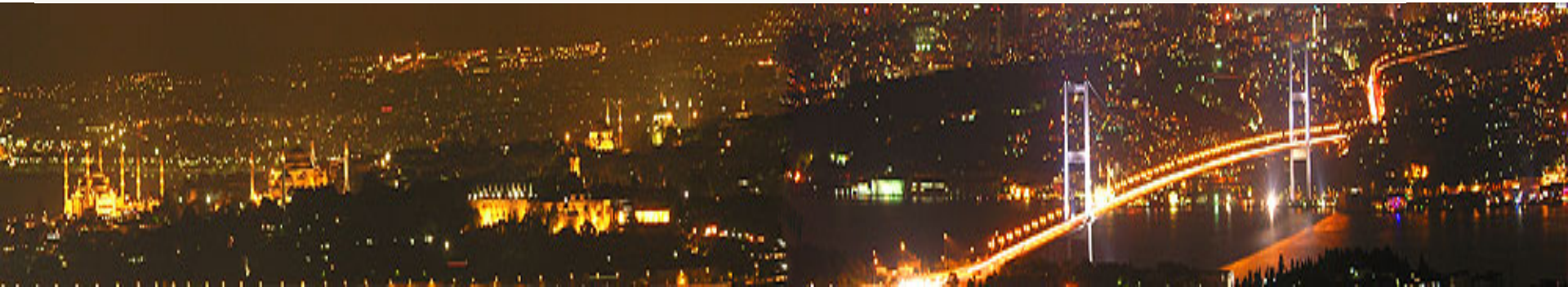


ATABAY

GROUP OF COMPANIES



Company Presentation



Istanbul, January 2015



AGENDA

1. Atabay Group of Companies Presentation

1. Overview
2. Chemical History
3. Atabay Pharmaceutical Products
4. Atabay Fine Chemical Products
5. Paracetamol Specifications

1.1 Overview

- ▣ Date: Founded in 1939 and still family owned by the Atabay family
- ▣ Sector: Pharmaceuticals and Fine Chemicals
- ▣ Category: Branded Generics and Active Pharmaceutical Ingredient
- ▣ Company:

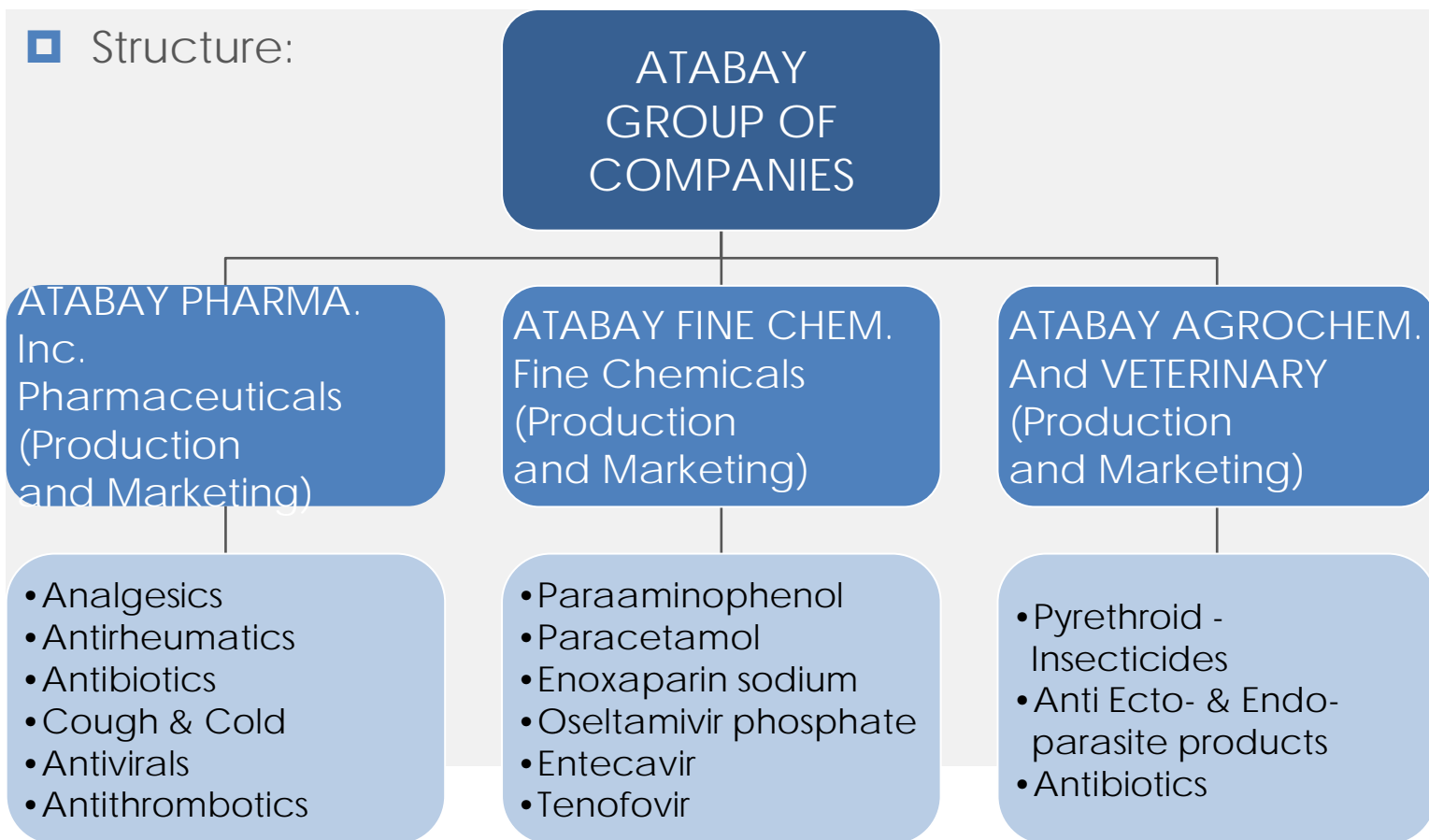
Employees	500
Medical Representatives	150
Manufacturing Personnel	300
Sales to Hospital Tenders and Wholesalers	
Sales to Finished Dosage Manufacturers	
- ▣ Market:

Home Market	Turkey
Export Markets	EU / USA / Russian CIS / Vietnam/ Iraq Afghanistan / Africa
- ▣ Philosophy: We care and feel responsible for your health

1.1 Overview

- ▣ Atabay Group consists of three main manufacturing and marketing companies situated at two sites:
- ▣ Site 1: Acibadem, Istanbul Site 2: Gebze, Istanbul
 - ▣ **Atabay Pharmaceutical Products, Inc.**
 - ▣ Production of a wide range of ethical and generic based pharmaceutical drugs, covering most therapeutic groups in nearly all dosage forms.
 - ▣ **Atabay Pharmaceutical Fine Chemical, Inc.**
 - ▣ Production of fine chemicals and intermediates for the pharmaceutical industry
 - ▣ **Atabay Agricultural Chemicals and Veterinary Medicines, Inc.**
 - ▣ Production of Active chemicals and formulations for agricultural and veterinary medicines for animal health.

1.1 Overview



1.1 Overview

Acibadem Plant:
10'000 m²



1.1 Overview

Gebze Plant:
300'000 m²



1.2 Chemical History

- Atabay's Chemical history goes back to 1970's and starts with the production of Paracetamol (Acetaminophen) and Aspirin (Acetylsalicylic acid). In the past forty years Atabay has produced more than fifty pharmaceutical or agricultural chemicals and has built plants for these products. By doing this Atabay has contributed to the solution of many human and veterinary health problems and very important agricultural issues.
- Atabay has benefitted from this experience and now has research labs where any pharmaceutical chemical product can be developed and produced.

1.2 Chemical History

▣ Examples of Pharmaceutical Fine Chemicals:

- | | |
|----------------------------------|---|
| ▣ P – Aminophenol | - Paracetamol precursor |
| ▣ Paracetamol | - Antipyretic analgesic |
| ▣ Acetylsalicylic acid | - Antipyretic analgesic |
| ▣ 6-APA 6-aminopenicillanic acid | - Ampicillin, Amoxicillin precursor |
| ▣ Phenylglycine | - Ampicillin side chain |
| ▣ N-(4-hydroxyphenyl) glycine | - Amoxicillin side chain |
| ▣ Ampicillin | - Antibiotic |
| ▣ Amoxicillin | - Antibiotic |
| ▣ Ibuprofen | - Anti – inflammatory antipyretic agent |
| ▣ Ethambutol | - Treatment of tuberculosis |
| ▣ Rifampizin | - Treatment of tuberculosis |
| ▣ Glycyrrhizid acid | - Antiulcer activity |
| ▣ Metformin | - Diabetis |

1.2 Chemical History

- ▣ Examples of Agricultural and Veterinary Chemicals:

- ▣ Herbicides:

- ▣ 2,4 D acid Wheat herbicide
- ▣ Trifluralin Cotton herbicide
- ▣ Propanil Rice herbicide

- ▣ Insecticides:

- ▣ DV.- acid chloride Pyrethroid insecticides interme
- ▣ Permethrin Pyrethroid insecticide
- ▣ Cypermethrine Pyrethroid insecticide

- ▣ Miticide:

- ▣ Amitraz Insecticide used for the control of all kinds of mites

1.3 Pharmaceutical Products

- Under our philosophy

„We care and feel responsible for your health“

Atabay produces around 100 pharmaceutical products with highest quality.

- Atabay produces a wide range of **consumer based pharmaceutical products** under its own brand label Atabay® for both the domestic and export markets. These products are presented in nearly all dosage forms, tablets and capsules to oral suspensions and suppositories.
- The entire production is conducted under full range of standard operational procedures, in order to guarantee superior quality in complete adherence to the current good manufacturing (cGMP). At the same time, Atabay continues to meet the stringent regulations and requirements of the WHO, FDA, and PIC.



1.3 Pharmaceutical Products

- ▣ Quality Management and Production

- ▣ Atabay has independent quality assurance (QA) and quality control (QC) departments with fully equipped laboratories and experienced as well as regularly trained staff

▣ Number of QC staff:	25
▣ Number of QA staff:	8
▣ Number of production staff:	300

1.3 Pharmaceutical Products

▣ Dosage forms

- ▣ Tablets
- ▣ Suspensions
- ▣ Syrups
- ▣ Suppositories
- ▣ Capsules
- ▣ Sachets

▣ Packaging Lines

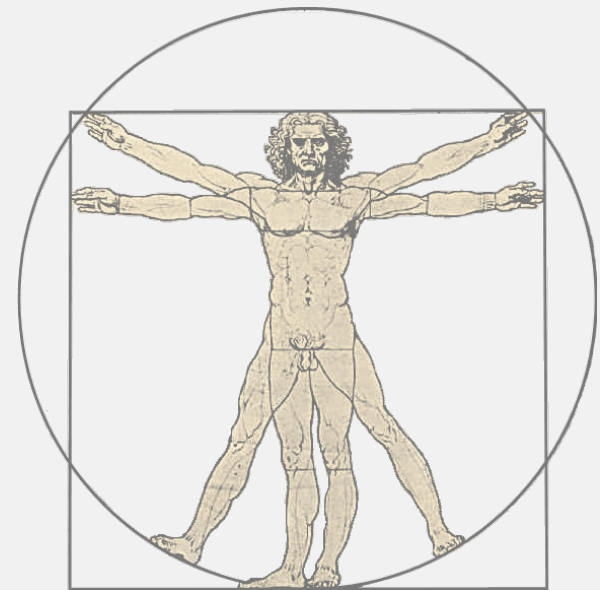
- ▣ ALU / ALU Packaging Line
- ▣ ALU / PVC Packaging Line
- ▣ Bottling Line
(Syrup –, Tablet –, Powder – Filling)
- ▣ Sachet Filling Line
- ▣ Prefilled Syringe Filling and Rod Inserting Line

Production Capacity is around 40 Million Units per Year with rising tendency

1.3 Pharmaceutical Products

▣ Atabay's product list covers following therapeutic fields:

- ▣ Analgesics / Cough and Cold Preparations
- ▣ Anti Rheumatics / Anti Inflammatory
- ▣ Mucolytic
- ▣ Expectorants
- ▣ Antibiotics – Antibacterials
- ▣ Floroquinolones – Antimicrobial
- ▣ Macrolides – Antibacterial
- ▣ Antitussives
- ▣ Antituberculosis / Antibiotics – Antibacterials
- ▣ Anti – Ulser
- ▣ Antihistamines
- ▣ Antiviral
- ▣ Antithrombotic
- ▣ Anti – Cancer



Leonardo da Vinci: „homo vitruvianus“ or „Manpower“

1.3 Pharmaceutical Products

- ENFLUVİR® 75 mg hard capsules
- ENFLUVİR 12 mg / ml Powder for Oral Suspension
 - Oseltamivir and Finished Dosage Forms are produced with the support of Ministry of Health. Flu epidemic in 2013 could be prevented with the help of national production of this substance by Atabay.



1.3 Pharmaceutical Products

- ▣ **Parol Infusion 1g/100 ml**
 - ▣ Used as analgesic/antipyretic in cases of intravenous application is necessary



1.3 Pharmaceutical Products

- ▣ **Enox – Syringes ready for use**
 - ▣ Used in thromboembolism treatments
 - ▣ First biotechnologic product produced by Atabay



1.4 Active Pharmaceutical Ingredients

- ▣ List of Fine Chemical Products produced at Atabay facilities
 - ▣ Paracetamol (Acetaminophen) Powder and DC Grades
 - ▣ Oseltamivir phosphate(USP/PH EU)
Treatment of influenza
 - ▣ Entecavir (USP/PH EU)
Treatment of chronic Hepatitis B
 - ▣ Tenofovir
Treatment of chronic Hepatitis B
 - ▣ Enoxaparin Sodium (USP/PH EU)
Treatment of thromboembolism
 - ▣ Esomeprazole
Treatment of ulcer
 - ▣ Zoledronic Acid
Treatment for bone desorption

1.4 Active Pharmaceutical Ingredients

■ List of Fine Chemical Products to be registered

Therapeutic Group	Material Name
Antifungal	Amphotericin B Caspofungin Acetate Posaconazole
Anti-neoplastic (oncology)	Imatinib Erlotinib Bortezomib Pemetrexed Capecitabine
Multiple Sclerosis (MS)	Glatiramer Acetate

1.4 Active Pharmaceutical Ingredients



1.5 API: Paracetamol/Acetaminophen

- ▣ Why Atabay as the main Paracetamol /Acetaminophen supplier:
 - ▣ Leading, dedicated Paracetamol / Acetaminophen Powder and DC grades manufacturer
 - ▣ One of the two fully entegrated manufacturers and only remaning European Manufacturer
 - ▣ Family owned and managed business since 1939
 - ▣ Extensive manufacturing history and experience
 - ▣ Flexible approach to customer specification
 - ▣ High quality (low impurities)
 - ▣ Strong regulatory compliance

1.5 API: Paracetamol/Acetaminophen

- Why Atabay as the main Paracetamol / Acetaminophen supplier:
 - Only European Manufacturer
 - Remaining bias towards Western/European supplier for reliability issues
 - Logistical service advantage over Asian based suppliers

1.5 API: Paracetamol/Acetaminophen

- ▣ Why Atabay as the main Paracetamol /Acetaminophen supplier:
 - ▣ Fully integrated manufacturer
 - ▣ Forward integration: Dosage manufacturing available
 - ▣ Backwards integration: PAP manufacturing
 - ▣ Increased security of supply
 - ▣ Complete control over impurities
 - ▣ Consistent PAP ensures consistent APAP
 - ▣ Future projects:
 - ▣ Further back integration to benzene

1.5 API: Paracetamol/Acetaminophen

- ▣ Brief explanation of the manufacturing process:
 - ▣ Bamberger Process
 - ▣ The manufacturing process starts from nitrobenzene, followed by catalytic hydrogenation using locally produced hydrogen to get Paraaminophenol.
 - ▣ Paraaminophenol is acetylated by acetic anhydride for producing Paracetamol/Acetaminophen.
 - ▣ The crude paracetamol produced this way is crystallized in deionised water and purified paracetamol/acetaminophen is obtained.
 - ▣ In this process halogenated aromatic compounds are not used, so formation of toxic halogenated aromatics like parachloroacetanilide is not possible.

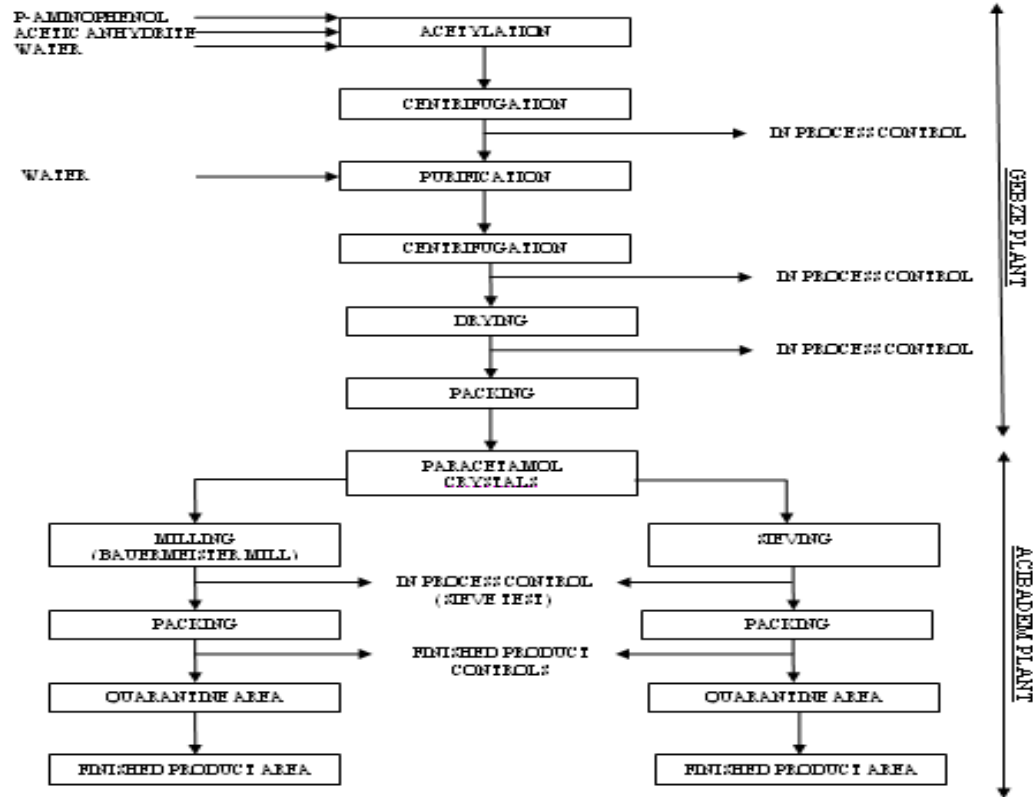
1.5 API: Paracetamol/Acetaminophen

- ▣ Brief explanation of the manufacturing process:
 - ▣ Only process to consistently yield low impurities
 - ▣ Hydrogenation versus iron reduction
 - ▣ Iron reduction discontinued in regulated countries
 - ▣ All Asian manufacturers use P-aminophenol manufactured by iron reduction
 - ▣ Regular tablet trials of all DC production

1.5 API:

Paracetamol/Acetaminophen

FLOWCHART OF PARACETAMOL POWDER PRODUCTION



1.5 API:

Paracetamol/Acetaminophen

PARACETAMOL/ACETAMINOPHEN PRODUCTION – QUALITY CONTROL

STABILITY TESTING



ASSAY and IMPURITY TESTING (HPLC)



1.5 API:

Paracetamol/Acetaminophen

PARACETAMOL/ACETAMINOPHEN PRODUCTION – SIEVE TESTING

Rotap Sieve Testing:

Performed during in-process and finished product testing.

Vibration Sieve Testing:

Performed during finished product testing.



1.5 API:

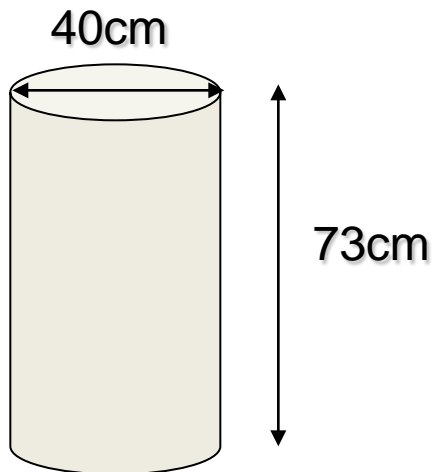
Paracetamol/Acetaminophen

PARACETAMOL/ACETAMINOPHEN PRODUCTION – RESIDUAL SOLVENTS

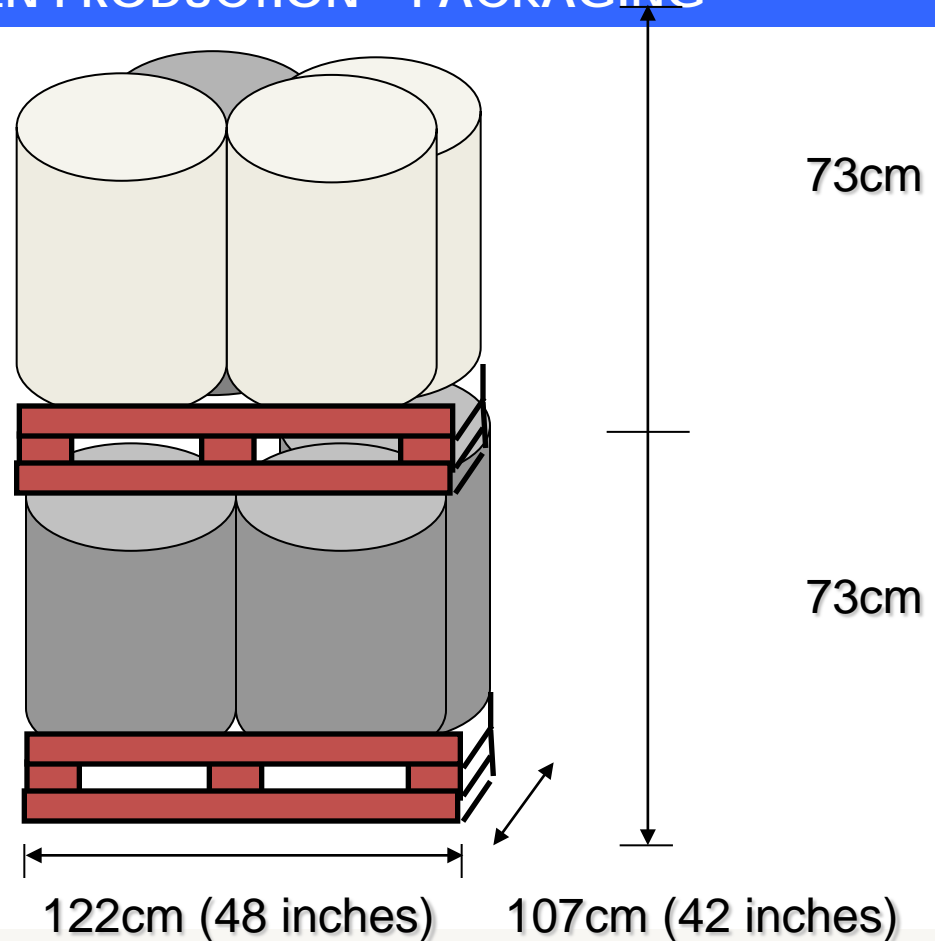
- WATER IS USED THROUGHOUT THE SYNTHESIS AND IN THE FINAL CRYSTALLISATION STEP
- ACETIC ACID IS TESTED DURING IN-PROCESS TESTING OF EACH BATCH OF PARACETAMOL/ACETAMINOPHEN WITH LIMIT OF MAX 0.5 % (POTENTIOMETRIC TEST WITH SODIUM HYDROXIDE)
- ROUTINELY LOSS ON DRYING TEST WITH LIMIT OF 0.5 % IS DONE ON THE FINAL PRODUCT (ACETIC ACID/CLASS III WITH MAX 5000 PPM)

1.5 API: Paracetamol/Acetaminophen

PARACETAMOL/ACETAMINOPHEN PRODUCTION – PACKAGING



Product is supplied in 50 kg net double-ply food grade PE-lined fiber drums.



1.5 API: Paracetamol/Acetaminophen

PARACETAMOL / ACETAMINOPHEN PRODUCTION – PACKAGING



ATABAY
KİMYA SANAYİ VE TİCARET A.Ş.

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PHONE : +90 216 326 65 33
FAX : +90 216 340 13 77
E-MAIL: info@atabay.com



**PARACETAMOL PH EUR/USP
FINE POWDER
(CODE APC 150)**

MADE IN TURKEY

BATCH NO:

NET 50 KG.

CAUTION STOW AWAY FROM SOURCES OF HEAT AND BOILERS.
FOR MANUFACTURING, PROCESSING OR REPACKAGING

1.5 API: Paracetamol/Acetaminophen

- ▣ Paracetamol (Acetaminophen) Grades:
 - ▣ Paracetamol (Acetaminophen) PH.EUR./USP Fine Powder (Code APC 150)
 - ▣ Paracetamol (Acetaminophen) PH.EUR./USP Extra Fine Powder (Code APC 152)
 - ▣ Paracetamol (Acetaminophen) PH.EUR./USP Micronized Powder (Code APC 154)
 - ▣ Paracetamol (Acetaminophen) PH.EUR./USP Crystals Capsule Grade (Code APC 162)
 - ▣ Paracetamol (Acetaminophen) PH.EUR./USP Sp Powder (Code APC 174)
 - ▣ Paracetamol (Acetaminophen) PH.EUR./USP Super Fine Powder (Code APC 176)
 - ▣ Paracetamol (Acetaminophen) PH.EUR./USP Powder (Code APC 178)
 - ▣ Paracetamol (Acetaminophen) PH.EUR./USP Purified Powder (Code APC 180)
 - ▣ Paracetamol (Acetaminophen) PH.EUR./USP Semi Fine Powder (Code APC 182)
 - ▣ Paracetamol (Acetaminophen) PH.EUR./USP Granular (Code APC 184)
 - ▣ Paracetamol (Acetaminophen) PH.EUR./USP Dense Powder (Code APC 186)
 - ▣ Paracetamol (Acetaminophen) PH.EUR./USP Standard Powder (Code APC 188)

1.5 API: Paracetamol/Acetaminophen

- Paracetamol (Acetaminophen) DC Grades:
 - Paracetamol (Acetaminophen) PH.EUR./USP 83 % DC (Code APC 210)
 - Paracetamol (Acetaminophen) PH.EUR./USP 90 % DC (Code APC 230 C)
 - Paracetamol (Acetaminophen) PH.EUR./USP 90 % DC/C (Code APC 230 CP)
 - Paracetamol (Acetaminophen) PH.EUR./USP 90 % DC/C (Code APC 230 CP-R)
 - Paracetamol (Acetaminophen) PH.EUR./USP 90 % DC (Code APC 230 C/MS)
 - Paracetamol (Acetaminophen) PH.EUR./USP 90 % DC (Code APC 230 C/MS) Fine
 - Paracetamol (Acetaminophen) PH.EUR./USP 90 % DC + 10 % Pregelled Maize Stach (Code APC 230 F/MS)
 - Paracetamol (Acetaminophen) PH.EUR./USP 96 % DC (Code APC 242 C)
 - Paracetamol (Acetaminophen) PH.EUR./USP 96 % DC (Code APC 242 C/MS)
 - Paracetamol (Acetaminophen) PH.EUR./USP 96 % DC + 4 % Pvp (Code APC 242 P)
 - Paracetamol (Acetaminophen) PH.EUR./USP 96 % DC + 4 % Pvp (Code APC 242 FP)
 - Paracetamol (Acetaminophen) PH.EUR./USP 97 % DC (Code APC 244)

Details of Regulatory Approvals

- ▣ FDA
 - ▣ Facility Establishment Number: 3002806424
 - ▣ DUNS number: 643448798

- ▣ Licence number from Turkish Ministry of Health:
 - ▣ 08/1991 for Gebze
 - ▣ 08/2004 for Acibadem

CEP and DMF status

edqm

European Directorate for the Quality of Medicines
Division Certification of Substances



Certificate of suitability
No. R1-CEP 1995-050-Rev 01

1 *Name of the substance:*
2 **PARACETAMOL**

3 *Name of holder:*
4 **ATABAY KIMYA SANAYI VE TICARET AS**
5 Acibadem
6 Köftüncü Sokak No 1
7 TR - 81010 Kadıköy, Istanbul

8 *Sites of production:*
9 **ATABAY KIMYA SANAYI VE TICARET AS**
10 P K 55 Esentepe Mevkii Tavsanlı Köyü
11 TR - 41400 Gebze, Kocaeli
12 **ATABAY KIMYA SANAYI VE TICARET AS**
13 Acibadem
14 Köftüncü Sokak No 1
15 TR - 81010 Kadıköy, Istanbul

16 **THIS CERTIFICATE SUPERSEDES THE PREVIOUS CERTIFICATE**
17 **R1-CEP 1995-050-REV 00**

18 After examination of the information provided on the manufacturing method and subsequent
19 processes (including purification) for this substance on the sites of production mentioned above,
20 TR - 41400 Gebze, Kocaeli and TR - 81010 Kadıköy, Istanbul, we certify that the quality of the
21 substance is suitably controlled by the current version of the monograph **PARACETAMOL**
22 no. 0049 of the European Pharmacopoeia, current edition including supplements.

23 In the last steps of the synthesis water is used as solvent.

24 The holder of the certificate has declared the absence of use of material of human or animal
25 origin in the manufacture of the substance.

26 The submitted dossier must be updated after any significant change that may alter the quality,
27 safety or efficacy of the substance.

28 Manufacture of the substance shall take place in accordance with the Good Manufacturing
29 Practice and in accordance with the dossier submitted.

30 Failure to comply with these provisions will render this certificate void.

Postal Address: 228 Avenue de Colmar (entrance rue Schertz) B.P. 907 – F 67029 Strasbourg Cedex 1
Telephone: 03.88.41.30.30 - Fax 03.88.41.27.71 – Web site : <http://www.pheur.org>

- Certificate of Suitability No:
1995-050-Rev 01
- valid
- US DMF : 6267
- December 2013

Contact

- ▣ Thank you for your interest in Atabay

- ▣ Atabay Group Of Companies

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