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# Aspen
# Investor Site Visit
# Port Elizabeth Facilities

**June 2014**

# Aspen

**Aspen has a proud heritage dating back more than 160 years.**

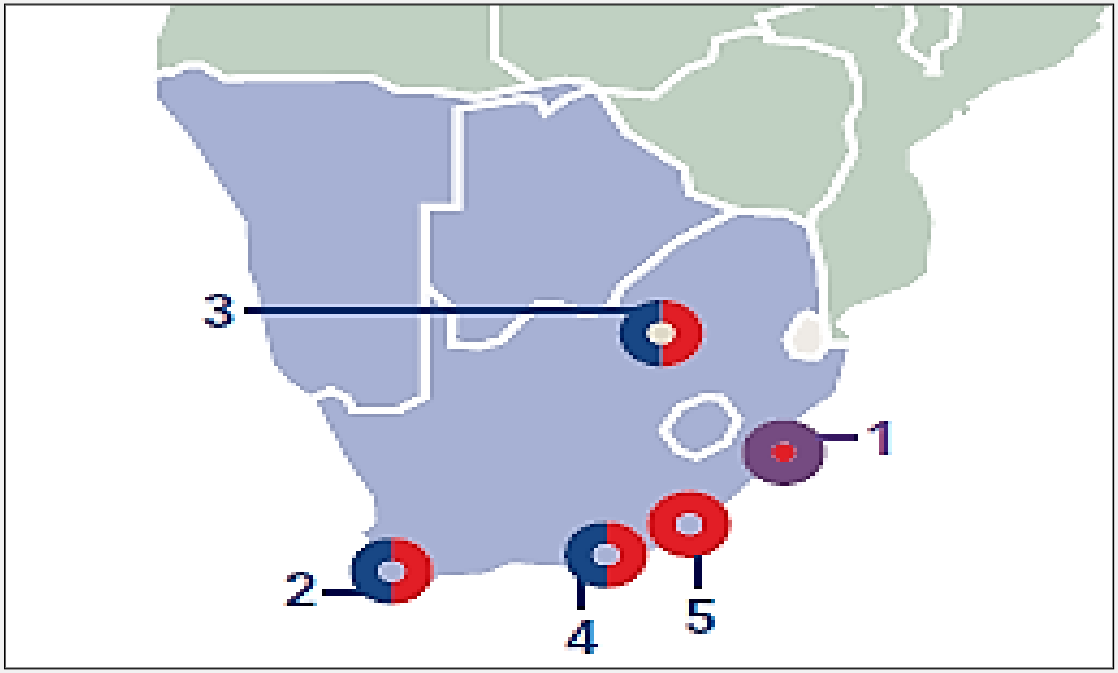
**The Group provides access to high quality, effective, affordable medicines and products in over 150 countries.**

# Strategic Manufacturing Partnerships

| | | | |
|---|---|---|---|
| Boehringer Ingelheim | **Boehringer Ingelheim** | Nevirapine |  |
| GSK GlaxoSmithKline | **GSK** | Lamivudine, Zidovudine, Combivir, Epivir & Others |   |
| Bristol-Myers Squibb | **BMS** | Stavudine, Didanosine, Atazanavir |      |
| GILEAD Advancing Therapeutics. Improving Lives. | **Gilead** | Tenofovir & Emtricitabine | Viread Truvada |
| MSD | **MSD** | Efavirenz |  |
| IROKO PHARMACEUTICALS, LLC | **Iroko** | Aldomet and Indocid |   |
| Lilly | **Eli Lilly** | Cycloserine and Capreomycin |    |
| BAYER | **Bayer** | Nur- Isterate Injection |  |
| PrestigeBrands Inc. | **Prestige Brands** | Murine & Murine Plus<br>Range of Eye Drop Products |   |

# Aspen's Global Footprint

# Aspen's South African Operations




- Group headquarters
- Combined sales, marketing, distribution and manufacturing centres
- Sales, marketing and distribution centres
- Manufacturing sites

| | |
|---|---|
| 1 | Durban, South Africa |
| 2 | Cape Town, South Africa |
| 3 | Johannesburg, South Africa |
| 4 | Port Elizabeth, South Africa |
| 5 | East London, South Africa |



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# Aspen Port Elizabeth Manufacturing Competitive Advantages

- **Proven Ability to Supply High Volumes of Products on a Reliable and Consistent Basis:**
  - The site has sufficient capacity to service existing markets and products that have been earmarked for transfer to the site.
  - Currently approximately 5.2 billion tablets and capsules are manufactured in Port Elizabeth, with a total annual capacity of 10 billion.
  - Focus on economies of scale - international volumes are being transferred to Port Elizabeth to reduce reliance on the public sector volumes.

- **Strong Focus on Quality and Excellence:**
  - The site is accredited by the South African and relevant international authorities.
  - The Quality Systems Management Review process ensures that the responsibility for quality is owned by each member of the management team.
  - The site has ISO 14001 and OHSAS 18001 accreditation.

- **Commitment to World Class Manufacturing and Supply to International Markets:**
  - The South African Operations Team has demonstrated their ability to manage product transfers and the supply of high quality, affordable products to international markets.

- **Competitive Procurement Strategies:**
  - Effective procurement strategies ensure that materials are purchased at competitive prices.

- **Focus on Continuous Improvement, Innovation and Technology:**
  - Focussed initiatives are in place with respect to resource conservation, improved production efficiencies and effective equipment operation.
  - The site was one of the first in South Africa to introduce bi-layer tabletting technology which is utilised in the production of triple combination tablets, e.g. Tribuss tablets.

# Evolution of Aspen's Manufacturing Base

- Aspen Heritage Facility in Port Elizabeth has been on the present site for approximately 70 years.
- Acquired by Aspen from South African Druggists in March 1999, together with facilities in East London and Johannesburg.
- Mainly supplied the South African market.
- Aspen has transformed from being a domestically accredited supplier to an international pharmaceutical manufacturer with the developed capability to supply various dosage forms to any pharmaceutical market in the world.
- Since 2005, more than R3.5 billion has been invested in the Group's South African facilities for infrastructural expansion and to ensure that the site meets the compliance standards of the relevant regulatory authorities in order to support Aspen's sustained supply to both its domestic and diverse international markets.
- Approximately 1700 people are permanently employed at Aspen's Port Elizabeth, East London and Nutritionals manufacturing facilities

# Aerial view of Aspen's Global Manufacturing Base in Port Elizabeth




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# Regulatory Authorities Relevant to South African Operations

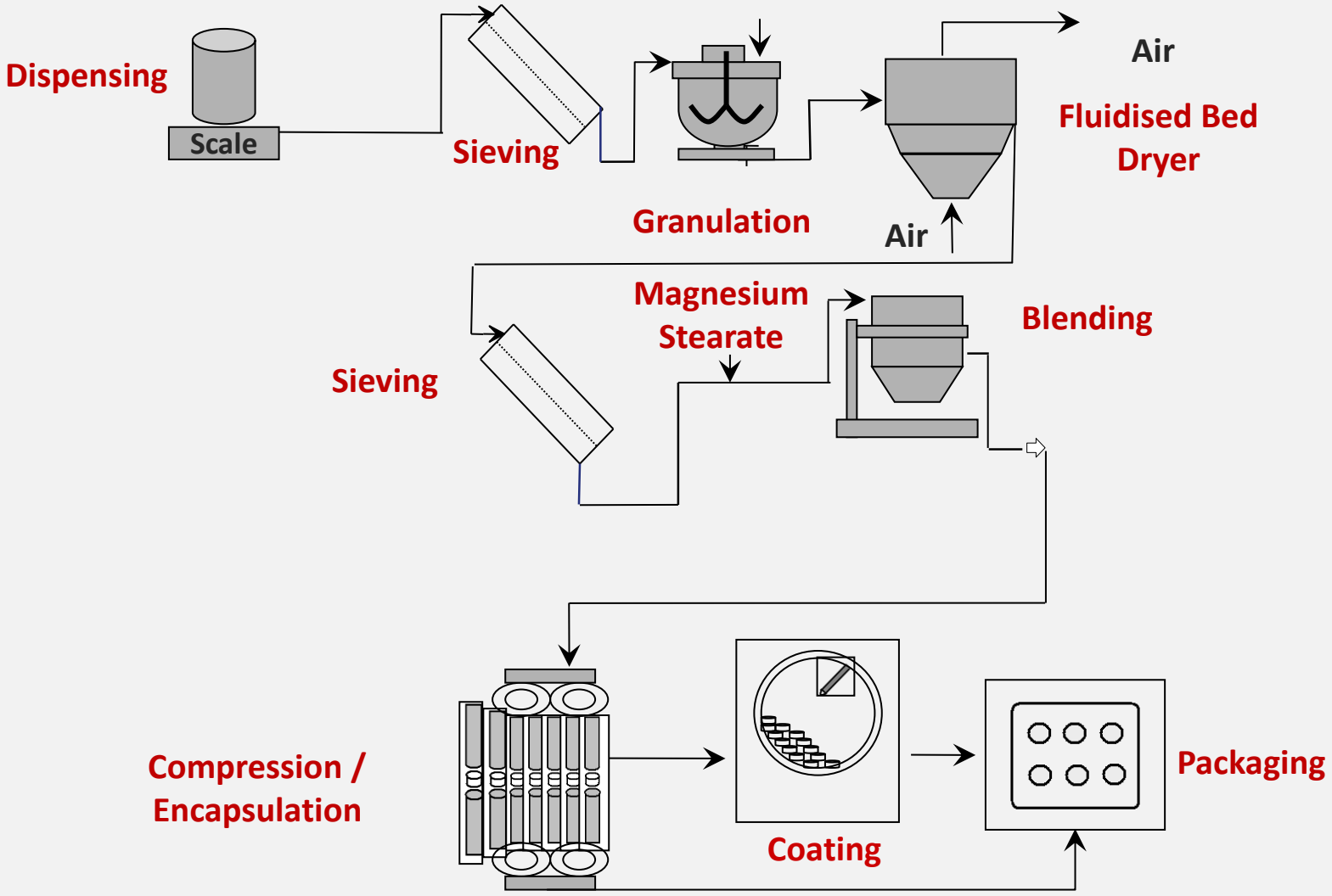
| Regulatory Authority | Unit 1 | Unit 2 | Unit 3 | SVP MP | SVP HP | East London | ADC | ACW |
|---|---|---|---|---|---|---|---|---|
| MCC (SA) | X | X | X | X | X | X | X | X |
| FDA (US) | X | X | | X | X | | X | |
| MHRA (UK) | X | X | | X | X | | X | |
| WHO | X | X | | X | X | | X | |
| TGA (Australia) | X | X | | X | X | | X | |
| Anvisa (Brazil) | X | X | | X | X | | X | |
| | High volume solid manufacturing for domestic and export markets | Small to medium volume solid manufacturing for domestic and export markets: fluid-bed dried products (2A) & oven dried products (2B) | End state solid packing for domestic market | Eye drops, lyophilized vials for domestic and export markets | High potency (incl. hormonal) injectables for domestic and export markets | Semi-solids, liquids and oral contraceptives for domestic market | Warehousing for domestic and export markets | Warehousing for domestic market |

**x = Approved**

# Unit 1 – Oral Solid Dosage Facility

- In 2005, an investment was made in the construction of an FDA-approved facility in response to the HIV/AIDS pandemic in Africa.
- Unit 1 currently manufactures 2.5 billion tablets/capsules, with the capacity to produce up to 6 billion tablets/capsules.
- This facility has been designed specifically for large batch sizes, high volume and low cost production of tablets (with bi-layer tableting capability) and hard gelatine capsules.
- The manufacturing facility contains state of the art equipment with automation and integration. The equipment has been installed in line with a “through the wall” design concept, which limits the amount of machinery in the primary manufacturing areas, and ancillary equipment is housed in a technical area.
- Process and material flows are optimised and material transfer is through gravity, vacuum and intermediate bin containers (IBCs).
- There are 3 main granulation processes :
  - Wet granulation - Fluidised Bed Drying (FBD) technology coupled to Granulators of varying capacities.
  - Dry granulation - Roller Compaction.
  - Direct compression – Milling and Blending.

# Flow Diagram of the Tabletting Processes



# Unit 1 – Oral Solid Dosage Facility

- The Unit 1 Packing capability includes:
  - Blister packing on three fully integrated blister lines of different capacities, with the capability of providing tamper evident, and uniquely identified individual packs on selected lines.
  - Bottle packing on three fully integrated lines of different capacities with serialisation (track and trace) on one bottling line developed in partnership with a 3rd party customer for export to China.



# Unit 2 – Oral Solid Dosage Facility


- In Jan 2009 a second oral solid dosage facility, Unit 2, was constructed in order to provide additional flexibility for smaller batch sizes and to provide static bed oven drying capability.
- The facility currently manufactures 2.5 billion tablets/capsules, with the capacity to produce up to 4 billion tablets/capsules.
- The facility can accommodate a wide variety of granulation batch sizes and contains a combination of oven drying and fluidized bed drying capability.



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# Unit 3 – General Facility

- Unit 3 is the original heritage facility which has been on the site in excess of 70 years.
- In line with the rationalisation strategy, a phased process for the transfer of products to other facilities in the group is in process:
  - Semi-solids (creams, ointments & suppositories) and Liquid Lennon Dutch Medicines have been realigned to the East London facility.
  - Tablets and Capsules have been realigned to Unit 1 and 2.
  - General Liquids are being realigned to the East London Facility.
- Packing for the local market is performed in Unit 3, the facility is being completely upgraded with new HVAC, finishes and fittings:
  - The project is being executed in 4 phases and phase 1 was completed June 2014.
  - The estimated final completion date for the entire project is May 2015.



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# Unit 4 High Containment Facility

- The facility will employ technologies that support the requirements for high levels of containment.
- Investment of R604 million.
- The facility will contain two dedicated and completely separate suites, namely the Hormonal Suite and the Oncolytic Suite.
- Construction of the facility is in progress and the scheduled completion date is January 2015.




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# The Steriles Facility

- Project commenced in 2007.
- Specialist facility for the manufacture of eye drops, lyophilised vials and sterile injectables, including hormonal vials and ampoules (a niche capability to supply female contraceptives and HRT products).
- The facility commenced with the production of eye drops for the US market in July 2009.
- Multi Product area is approved by the MCC, USFDA, TGA (Australia) and ANVISA (Brazil) for the manufacture of sterile eye drops and lyophilised vials and by the WHO for lyophilised vials.
- The Hormonal area is approved by the MCC, TGA and ANVISA for the manufacture of hormonal sterile ampoules and vials.
- The lyophilised vials area was commercialised in September 2010.
- The sterile facility represents a niche manufacturing capability.

# Steriles Facility – Multi-Product Suite

**Lines 1 and 2**

- High volume eye drops with an annual capacity of 42 million units.
- In excess of 30 million units being exported to US and Canada under a manufacturing contract with Prestige Brands.
- 2.5 million units of the Aspen's Eye Gene range have also been transferred to the facility.

**Line 3**

- Lypophilised vials have been introduced into this area, starting with Capreomycin, a product for MDR TB, which will be launched into Brazil in early 2015.
- Capacity for lyophilised vials is approximately 2.4 million units.
- Additional capacity exists for 2.9 million liquid filled vials and the transfer of a liquid biological product ex GSK is planned for mid 2015.

# Steriles Facility – High Potency Suite

**Line 4**

- High volume ampoule filling capability for hormonal injectables - a niche capability for filling and packing oily solutions.
- Annual capacity for 30 million ampoules.
- Validation batches of Bayer Nur-Isterate have been completed. Commercialisation of the Bayer Nur-Isterate product is imminent.
- Trial and validation batches of a range of male steroid hormones are currently in progress.

**Line 5**

- High volume vial filling capability for hormonal injectables, with a unique aseptic suspension filling capability.
- Annual capacity for vial filling of approximately 45 million units.
- Aspen's Medroxyprogesterone is envisaged to be manufactured for SA, emerging markets and WHO territories; a global formulation is being developed for world wide supply.

# East London Site

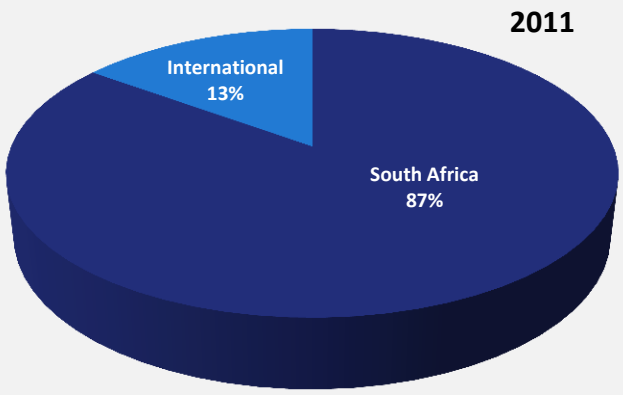
# East London Multi-Purpose Site

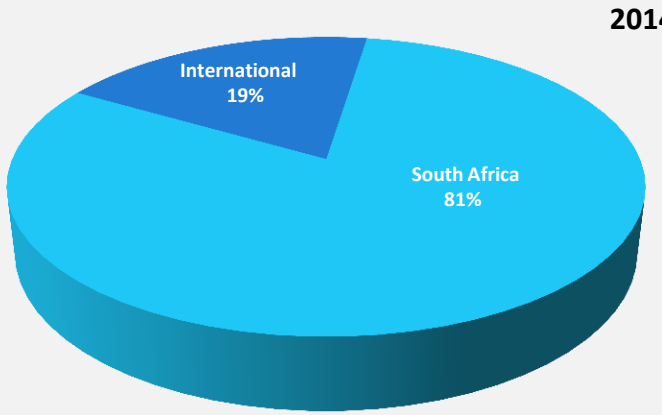
**General Facility**

- Highly flexible, small volume, solids manufacture, including low dose drugs.
- The East London facility is the centre of excellence for the production of liquids and semi-solids.
- Since 2009 Aspen has invested R228 million in projects to upgrade the East London Facility. The main upgrade projects included:
  - Low Bioburden creams and ointments: R29 million.
  - Lennon Dutch Medicines: R49 million.
  - High Volume Liquids: R66 million.
  - Finished Goods Warehouse: R18 million.
  - General Liquids: R56 million.

- The Oral Contraceptive Facility provides a contained manufacturing area for the production of high volume oral contraceptives for the public and private sector.

# Port Elizabeth Manufacturing: Growth in International Volumes




- Aspen Australia Products have been realigned Port Elizabeth:
  - 24 SKU's have been commercialised.
  - 25 SKU's are in the process of being transferred with approval anticipated during the 2014/2015 financial year.

- The manufacture of the Zyloric global brand has been realigned to Port Elizabeth. Europe, Malaysia, Singapore, South Africa and Chile are supplied from this facility, with launches into Latin America, MENA and French West Africa in process.

- Additional international volumes for selected markets are in the process of being introduced to the Port Elizabeth facility.

- The Prestige eye-drop range has been expanded through collaborative development between Aspen and Prestige.

- Prestige are also registering these products in new markets, including Taiwan and other South East Asian Countries (various stages of registration); these international volumes will be supplied from the SVP facility.

# Keys to Performance

- Leadership
- Attention to detail
- Planning and execution
- Continuous Improvement
  - Philosophy: There is value to be extracted from every activity/area of the business.
    *Everything can be done better, smarter, faster.*
    *Just because it works, it does not mean it can't be better.*
  - Ownership: Everyone is responsible for continuous improvement, not just management.
  - Systematic, logical approach:
    i. Identify and measure sources of inefficiency and waste/loss.
    ii. Identify alternative working methods, controls, technology, etc.
    iii. Prepare specific/detailed action plans with outcomes and target dates.
    iv. Drive, manage and measure outcomes of action plans.

# Milestones and Continuous Improvement Initiatives - Engineering, Safety, Health and Environment

- SA Operations achieved ISO 14001 and OHSAS 18001 accreditation in 2013.
- Sophisticated air handling systems are in place to purify and filter the air discharged from the production areas.
- Aspen achieved a CDP score of 87C in 2013 compared to 72D in 2012, and 63E for 2011. This is against an average score of 79C for the Healthcare sector and 83C across the Top 100 JSE companies for 2013.
- Significant resource conservation has been achieved in the past year and long term resource conservation plans are in place.
- The Disabling Frequency Ratio of 0.64 against a tolerance of 1.00 demonstrates the effectiveness of safety standards at the facilities.

# Continuous Improvement Initiatives – HR

- **Individual and Team coaching and mentoring**
  **Orientation to Management leadership development programme**
  ***Impact:*** *Empowered leadership – improved productivity*

- **Sick absence management through Return to Work interviews and absence trending/intervention**
  ***Impact:*** *Absenteeism reduced to below 2% - saving in labour cost*

- **Proactive interaction and engagement with Trade Unions, Works Councils and employees**
  ***Impact:*** *Improved employee engagement and increased output*

- **Automation of HR administration process via CRS and Org-Plus**
  ***Impact:*** *Faster processes with fewer resources*
  *On-line performance management*
  *On-line leave and IR management*
  *On-line wellness management*
  *On-line recruitment and termination management*



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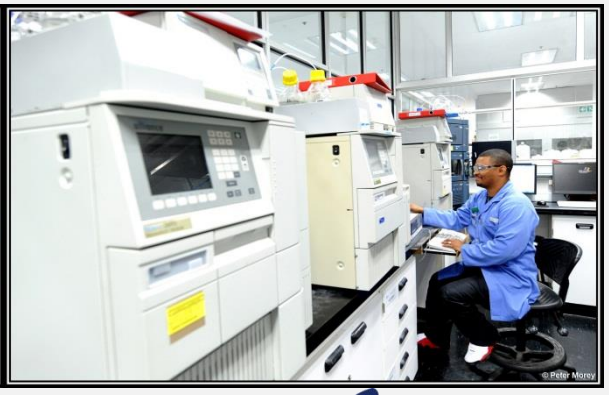
# Continuous Improvement Initiatives – Quality Control Laboratory

- **Raman technology (Truscan Laser Spectrophotometry)**
  ***Impact**: Direct testing on material receipt*
  *Reduced sampling and labelling*
  *Reduced handling – at point of receipt*
  *Reduced laboratory testing – immediate identification vs. laboratory test*

- **Vendor management**
  ***Impact**: Reduced sampling and laboratory testing of materials*

- **Test method conversion from HPLC to UPLC**
  ***Impact**: Reduced method run-time and reduced solvent usage*



# Continuous Improvement Initiatives – Production and Warehousing

- **Doubling of batch sizes to reduce set-up time between batches and thereby optimise equipment utilisation**
  ***Impact**: Reduction of total annual set up time by 50%*

- **Improved compression set-up and run-rate parameters**
  ***Impact**: Increased run rates of 20% achieved*

- **Standard manning and line balancing of packing lines**
  ***Impact**: Increased output*

- **Automation of end-of-line packing to match the increased rate of manufactured output / manual packing processes transferred to automated equipment**
  ***Impact**: 30% Output improvement in patient-ready packs*

- **Electronic batch records**
  ***Impact**: Improvement in documentation flows and audit close out*

- **Barcode inventory management system in warehousing and production dispensing**
  ***Impact**: 16% Reduction in headcount*

- **Barcode status labelling of materials implemented to reduce handling activities**
  ***Impact**: More efficient process through an instantaneous scanning process*

# Continuous Improvement Initiatives – Production and Warehousing

- **Use of multi-tip tooling in tablet compression**
  ***Impact**: Increased run rates*

**Table showing improvement in efficiencies using multi-tip tooling:**

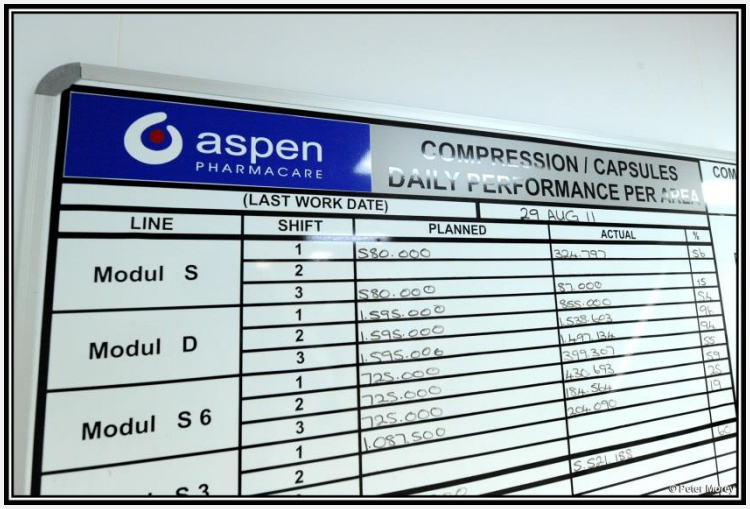
| Product | Previous Rate | Current Rate | % Increase |
|---|---|---|---|
| Zyloric 100mg | 120000/hour | 240000/hour | 50% increase |
| Panamor 50 mg | 135000/hour | 266000/hour | 49% increase |
| Ridaq 25mg | 276000/hour | 455000/hour | 40% increase |
| Phenerine | 108000/hour | 162000/hour | 33% increase |
| Trepiline 25mg | 107000/hour | 414000/hour* | 74% increase |

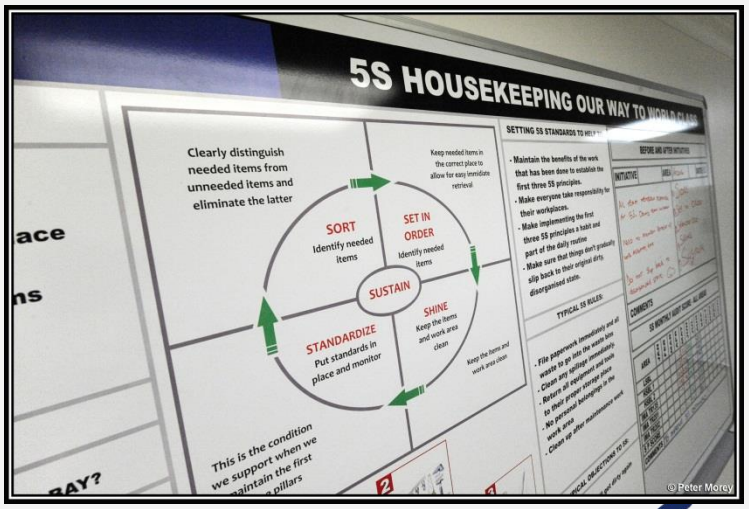
# Continuous Improvement - Impact on Expenses

- For the 2013/2014 financial year, as at April 2014, SA Operations (PE, SVP, EL and Nuts) achieved savings to the value of R36.6m.

- Continued improvement savings achieved for Port Elizabeth:

  - Unit 1 Solids Manufacturing: R7.2m
  - Unit 1 Solids Packing: R12.5m
  - ACW R7.7m
  - Procurement R3.6m



# Continuous Improvement - Procurement

- Comprehensive understanding of products / materials, driving factors and market factors.
- Ability to effectively benchmark product prices, quality and supplier service to ensure that we are procuring optimally.
- Longstanding relationships have been established with international API and packaging suppliers.
- Ability to source competitively from developing markets.
- Only reputed and validated suppliers are approved for use.
- Alternate suppliers are in place to mitigate supply risk and leverage pricing.

# SA Operations Competitiveness

## PE vs. Global 3rd Party Suppliers (ex works)

| | Other material | Conversion | Total |
|---|---|---|---|
| Average Reduction *(based on a sample of 16 SKUs)* | -20% | -44% | -40% |

## PE vs. Sigma (ex works)

| | Other material | Conversion | Total |
|---|---|---|---|
| Average Reduction *(based on a sample of 28 SKUs)* | -46% | -62% | -53% |



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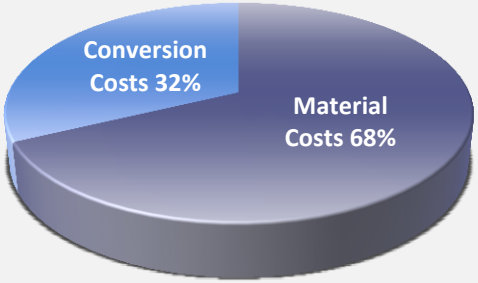
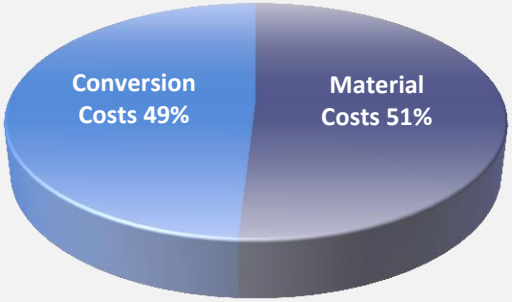
# In-house Manufacturing Cost Analysis

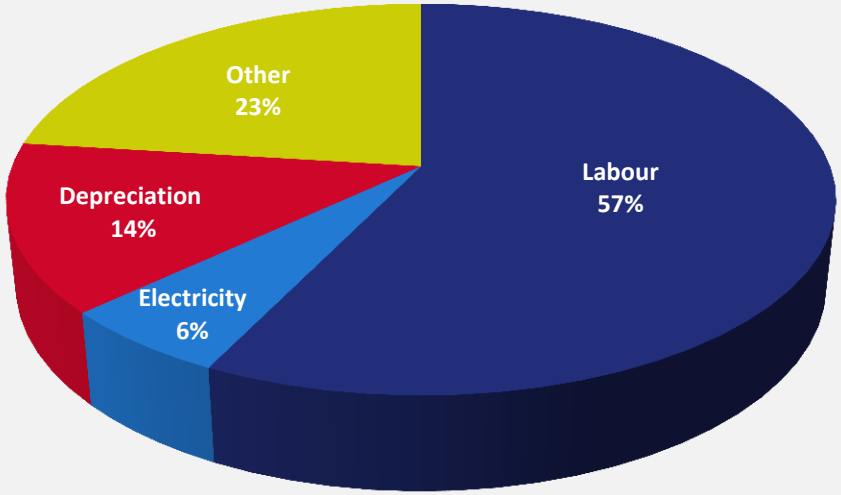
## Allocation of Production Costs (Including ARV's)




## Allocation of production Costs (Excluding ARV's)




## Allocation of conversion costs



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# Training and Development

- Aspen has  training programmes in place across all levels of the business, to support operational requirements.

- The following training initiatives were successfully completed by employees in the 2013 and 2014:
  - Business Practice: 19 employees.
  - Warehouse Practice: 15 employees.
  - Pharmacist Assistant Basic: 21 employees.
  - Pharmacist Assistant Post-Basic: 21 employees.
  - Aspen Business Management Programme: 13 employees.
  - Diploma in Production Management: 10 employees.
  - Analyst in-service training: 13 employees.
  - Electrician trade test: 1 employee.
  - Women in Leadership: 20 employees.
  - Pharmacist Internships:  10 employees.

- Bursaries were awarded to 50 employees during the 2013/2014 financial year.


# Risks and Challenges

- **Realisation of awarded public sector volumes**

  ***Mitigation:*** *International volumes are being introduced to Port Elizabeth*

- **Impact of inflation and currency movements on cost of goods**

  ***Mitigation:*** *Benefits from continuous improvement initiatives and effective procurement strategies are being realised*

- **Increased competition from foreign suppliers**

  ***Mitigation:***
  - *Cost of goods are benchmarked against international prices*
  - *Aspen's successful performance in the recent ARV tender demonstrates competitiveness*
  - *Aspen has proven to be a reliable supplier*
  - *Significant investment has been made in creating flexible and diverse manufacturing capability to respond to current and future requirements*

# Conclusion

***Our world class South African Operations team has created Aspen's sustainably efficient and competitive manufacturing platform.***