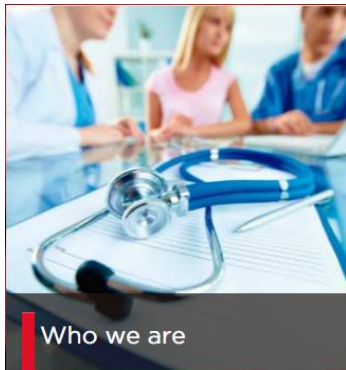




German Payer Evidence - A Case Study

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German Law - AMNOG

The Law on the Reorganization of the Pharmaceutical Market (German abbreviation: AMNOG) became effective on January 1st, 2011. Module 4 requires a systematic overview regarding the (additional) medical benefit (description of the methodology and results) and indication of patient groups with an additional benefit.

General Approach

The statistics and programming is quite different from traditional clinical study reporting of safety and efficacy in support of regulatory approvals. Proof of additional benefit requires different types of tables, statistical modeling, studies, etc.

Scope of Work

- Studies: $n = 4$
- Populations: $n = 1$
- Sub-populations: $n = 11$
- Endpoints: $n = 33$
- Time points: $n = 4$
- **Potential tables: $n = 5000$**
- **Actual tables: $n = 1000$**

Requirements

- Minimize new coding by reusing prior SAS code
- Use of Word documents for maintaining TFL specification
- Use of Excel spreadsheets for tracking
- Delivery of PDF's having bookmarks and hyperlinked TOC

Statistical Considerations

- Approval of statistical SAS code
- Review of output when numbers become small
- Change of statistical procedures based on output
- Change control of sub-populations

Programming Challenge

- One study had 8 sub-populations that used the same SAS code.
- Each sub-population could affect previous programming.
- Changes to any one sub-population would require all sub-population programs to be changed and re-run.

Programming Solution

- Write one set of programs for sub-population #1
- Copy programs for each sub-population from sub-population #1
- All changes were made to sub-population #1 programs
- Program using regular expressions controlled versioning

Timelines & Resources

- Originally wanted all tables delivered in two weeks
- Agreed to receive tables in batches
- Agreed to receive overall tables – easier to QC, followed by sub-group tables
- Four programmers worked 6 months

Sub-population Scope Changes

- Baseline medications
- On treatment medications
- Time periods
- Treatment dependent rules

TFL Scope Changes

- Different models for p-value calculations
- Representation of missing values for small n's
- Title changes
- Additional explanatory footnotes
- Number changes to match prior submissions

Tracking

- Excel Files for tracking
 - Programs and Quality Control
 - Issues
 - Deliveries
 - Timelines

Naming and Copying Programs

- Program name and content coordination
- Use of regular expressions to create programs copies
- Iterative QC approach
- Deliver overall tables first then subgroups to accommodate timelines

Quality Control

- Double programming
- Comparison of numbers to previous submission output where applicable
- Independent programming by Statistician
- Review by German Payer team

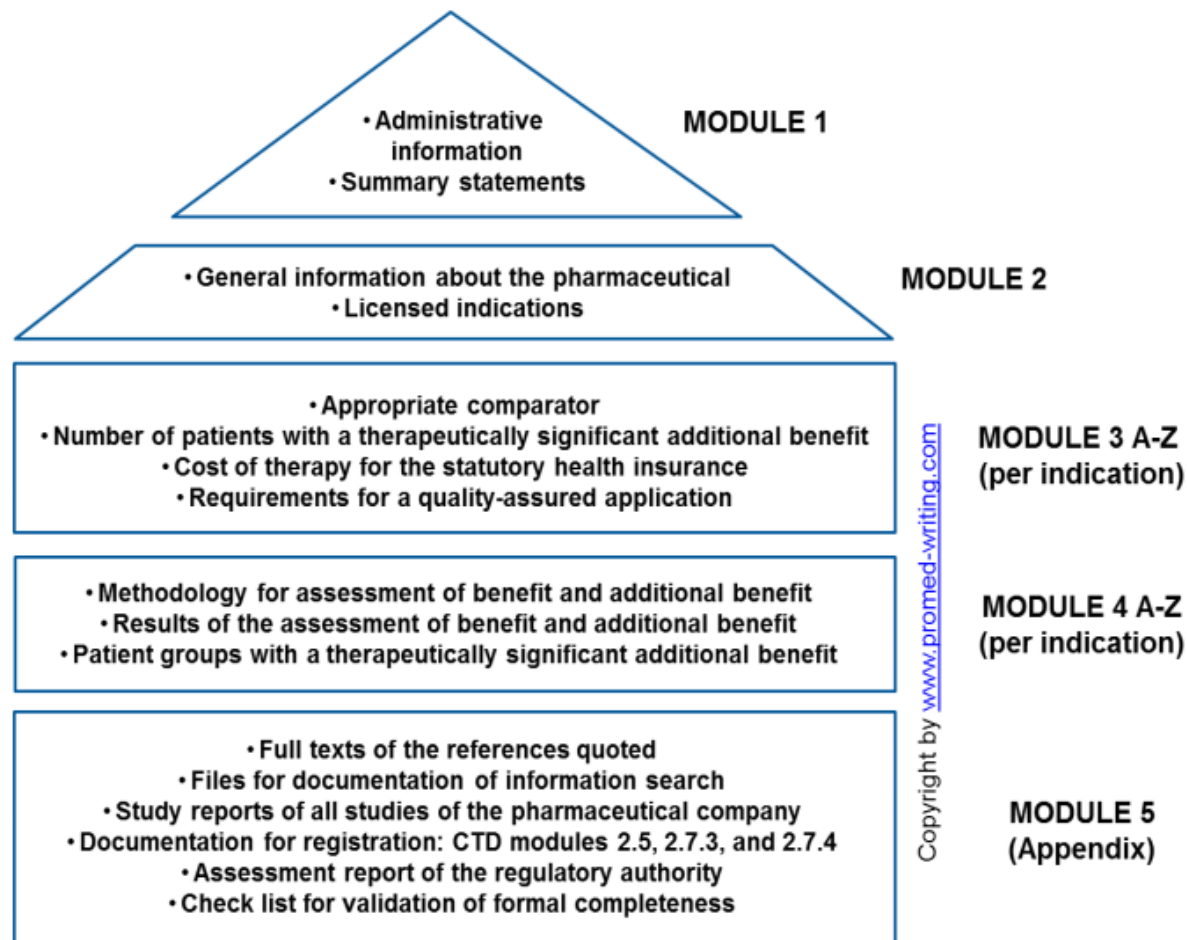
Programming Deliverables

- 1000 tables were programmed
- Due to changes, 3000 outputs were provided
- All output was in PDF format
- Transfer of files occurred through FTP service
- Audit logs and versioning were maintained

Final Delivery

- Value dossiers for 2 Products
- Value dossier (Modules 1-4)
 - Product 1 consisted of 2,568 pages
 - Product 2 contained of 1,319 pages

Dossier



Classification

	Classification
1	Major
2	Significant
3	Minor
4	Not quantifiable
5	No additional benefit documented
6	Benefit lower than the use of the ACT

Thank You

German Team

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Statistics and Programming Team

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