

## **Arezzo® Technical White Paper**

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## 1. Clinical guidelines and care protocols

With medical knowledge expanding at an exponential rate, physicians struggle to keep pace with all of the information required for the delivery of care. Furthermore, the range of diagnostic and therapeutic options is expanding. Various health professionals often look after the same patient across multiple settings. These issues increase the risk of duplicated effort, mistakes and inappropriate care. Guidelines and protocols, which describe best practice in specific areas of medicine, are used to facilitate safe, cost-effective patient management.

Computers can assist in providing guidelines, protocols and other information at the point of care. With an electronic medical record, there is the possibility of linking patient data with these aids. Unfortunately, guidelines and protocols often cannot be personalised to an individual patient. Published documents, whether in html or PDF formats must cover all or most of the cases that arise, and thus contain more information than is pertinent to a particular case. This leaves the clinician having to sift out the extraneous content and then apply what is relevant.

Ideally, electronic guidelines and protocols should also be flexible enough to accommodate the complex work patterns of clinical practice, without compromising the goal of appropriate care. Even within the same institution, there may be variations in a care protocol that are dependent on who is using the protocol in what part of the institution. Clinician compliance is further reduced when protocols cannot be customised to these variations, where appropriate.

Authoring a text-based guideline or care protocol is time-consuming. Significant intellectual effort is needed, which is then wasted if the protocol is not used or cannot be updated easily. The problem is considerable: how to create guidelines and care protocols that can be personalised to each patient, that can accommodate appropriate variations in work patterns, and still be created in a cost-efficient way.

## 2. What is Arezzo®?

Arezzo® is a software technology that can be used to create and run clinical guidelines and care protocols.

Arezzo® has been developed over 10 years in the Advanced Computation Laboratory of the Imperial Cancer Research Fund, a major cancer research charity in the United Kingdom. This research and development has resulted in a technology that can:-

- Mimic the way human experts make decisions by:
  - Providing options for each decision
  - Producing clearly defined arguments for and against all options, including those options that are not recommended
  - Personalising the arguments according to the specific circumstances in which a decision is being made
- Handle clinical uncertainty in decision-making. The argumentation approach does not require probabilities or numeric weighting for decision support. This information is frequently not available, thereby limiting systems that use Bayesian reasoning.
- Enable decisions within the context of executable guidelines and protocols
- Deliver patient-specific views of guidelines so that users only interact with the pertinent information in a guideline or protocol. Irrelevant information is kept in the background.

- Be ‘pro-active’, able to provide prompts and reminders of what needs to be done next for this patient, and when.
- Provide simple-to-use tools for creating the knowledge base needed for guidelines, protocols and decision-making and for detecting logical inconsistencies in the knowledge base
- Minimize time spent at the computer. Arezzo’s robust, highly efficient inference engine can rapidly process the knowledge base and stored guideline, and guidelines can be encoded so as to minimize the number of questions asked of the user.
- Utilise a declarative approach, which means:
  - The knowledge and behaviour of any guideline is clearly defined
  - Guidelines are flexible and can be adapted to the needs of various users.

Arezzo® comprises three components:

- Guideline authoring tool (**Composer**) – which is used to create executable guidelines and care protocols. The Composer has undergone continuous improvements to ensure the rapid authoring and deployment of clinical guidelines and protocols.
- Guideline testing tool (**Tester**) – which enables testing of guidelines before deployment
- An inference engine (**Performer**) – which runs the Arezzo® guidelines and care protocols at the point of care. The Performer engine has been optimised for reliability and speed of running guidelines.

Figure 1. provides an overview of the Arezzo® technology:

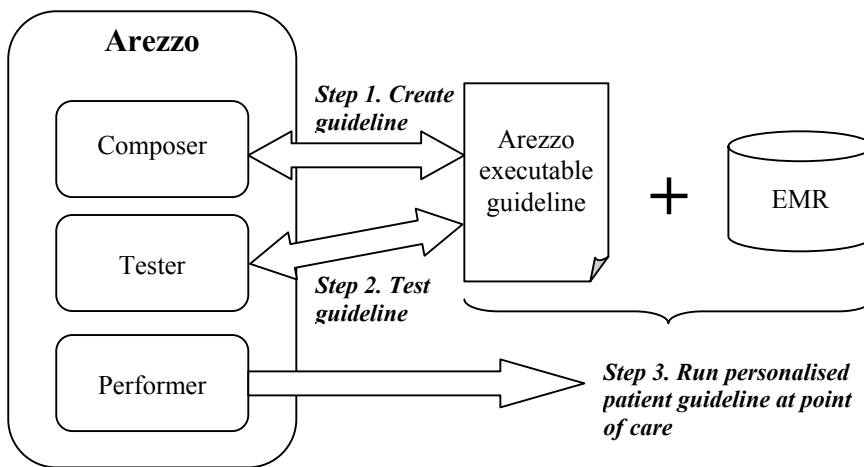


Figure 1.

### 3. How Do You Use Arezzo® Composer?

The Arezzo® Composer is used to create guidelines, protocols and care pathways. It provides a method for specifying clinical guidelines and protocols in terms of:

- **Tasks** and collections of tasks
- **Data items**
- Task and data item **attributes**

### 3.1 Tasks

There are four types of tasks:

1. **Enquiries** – request data. The requests can be sent to an electronic medical record or the person who is using the guideline.
2. **Decisions** - prompt the user with options for each decision. The options may be a list of interventions, differential diagnoses or possible actions. Each option will have supporting arguments for and against the option. The arguments will be customised to the individual patient. The clinician can weigh up the pros and cons for each option, while still being able to exercise clinical judgement.
3. **Actions** – are procedures to be carried out. These procedures may include presenting information or instructions to the user, sending emails or pager messages, or calling up other computer programmes.
4. **Plans** – provide a way of organising collections of the other tasks.

#### 3.1.1 Task States

During enactment of an Arezzo® guideline, each task will have a current **task state**. Examples of task states include:

1. **Dormant** – which means that the task has not yet been started. This is the default state for all tasks before the guideline is started.
2. **In progress** – when a task has become activated.
3. **Requested** – when an Enquiry task is activated and data values are sought for source data items.
4. **Established** – for any task that will become active after a pre-specified time interval
5. **Performed** – when a task instance is completed

### 3.2 Data Items

Data items are used to store data values collected during the running of a guideline. There are several types of data item, including:

1. **Text** – including free text typed in by the user, single-choice text values and multiple-choice text values.
2. **Integers**
3. **Real numbers**

#### 4. **Date/time**

#### 5. **Boolean** – true/false values

### 3.3 **Simple Arezzo® Example**

A simple example of an Arezzo® guideline that uses all of the task types is illustrated in Figure 2 below:

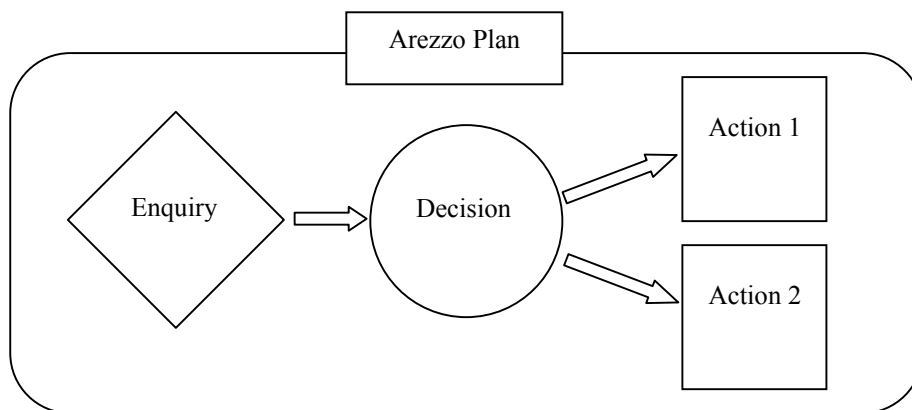


Figure 2.

If this example were run by the Arezzo® Performer engine, then the Enquiry task might request data about a patient’s clinical signs and symptoms. After this information was received, the Decision task would process the data values and then recommend options. Depending on which option the user chose, the guideline would then present the appropriate Action task. An example of this type of guideline can be viewed at online at <http://www.infermed.com/era>, which is an early cancer referrals application for use by family physicians.

Arezzo® guidelines can include multiple collections of the different task types. This means that complex clinical care protocols and guidelines can be created and run.

### 3.4 **Attributes**

All Arezzo® tasks and data items have **attributes** that define their properties and determine the behaviour of the guideline during enactment by the Arezzo® Performer engine.

Task attributes include:

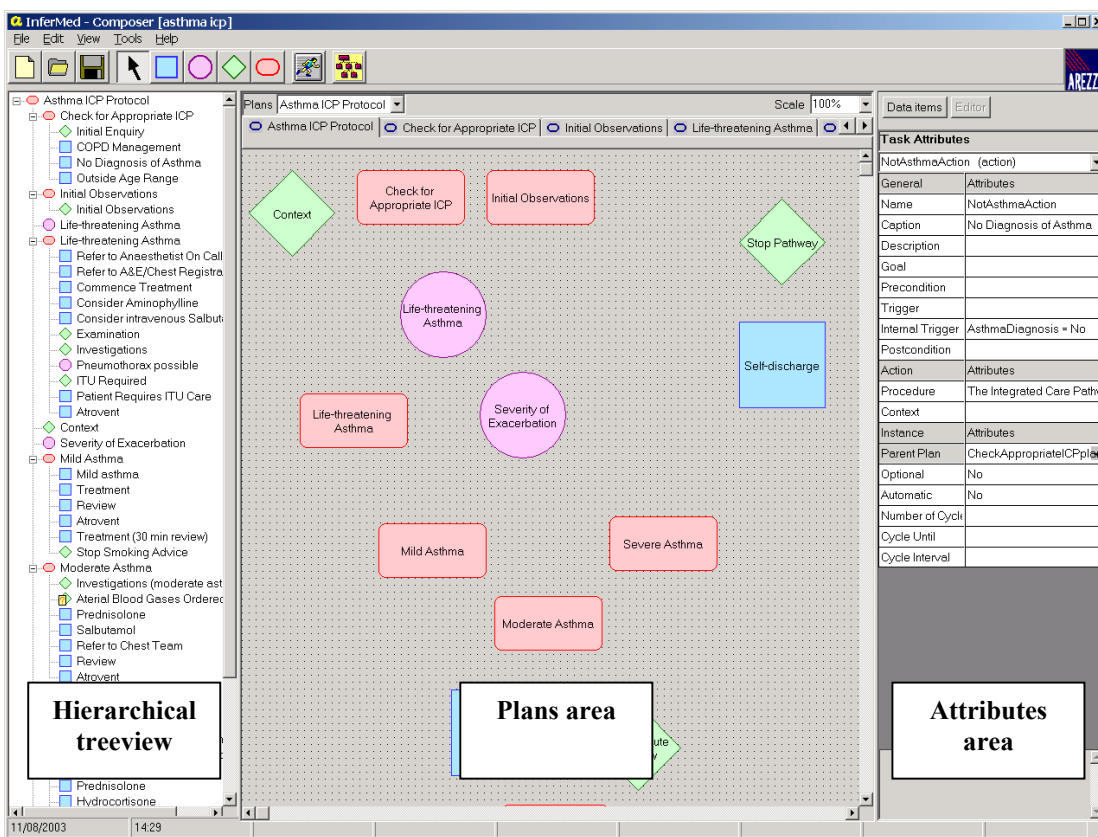
1. **Name** – the unique name for each task
2. **Description** – information about the task
3. **Internal Trigger** – an Arezzo® rule or expression that must be true for the task to be activated. Examples of internal triggers would include the completion of another task, the result of a decision, or certain pre-defined data values.
4. **Goal** - represents the purpose of the task. During guideline enactment, if a task is ready to be activated and its goal is true then the task will be skipped.

5. **Number of Cycles** – will cause a task to be repeated for the specified number of cycles. This attribute is useful for repeating tasks such as regular monitoring of blood pressure.
6. **Cycle Until** – can contain an Arezzo® rule or expression which, if true, will cause a cycling task to stop cycling. For example, an Enquiry task for monitoring blood pressure might continue cycling until the data value for the last blood pressure measurement is less than 120/80 mmHg.
7. **Cycle Interval** – determines how frequently a task will cycle. This can be seconds, minutes, days, weeks, months or years.

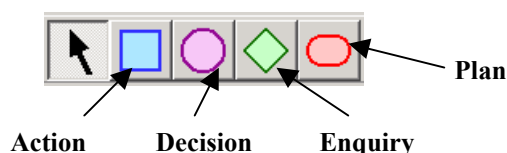
### 3.5 Using Arezzo® Composer to Create a Guideline

Arezzo® Composer is a Visual Basic application that can be launched from the Windows Start menu.

Composer has a three-pane screen, with a hierarchical tree view of the guideline tasks in the left pane, task-authoring tool in the middle pane, and the attributes-authoring tool in the right pane:



To create a new task, the guideline author just has to select one of the task icons from the Composer’s toolbar:



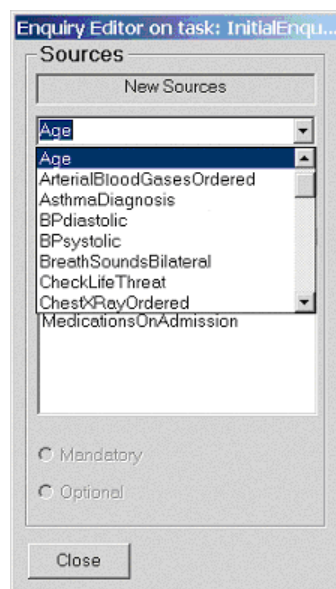
and place the icon onto the Plans area.

The author then uses the Attributes area to set the various properties of the task.

There are several additional tools that help the guideline author:

### 3.5.1 Enquiry Editor

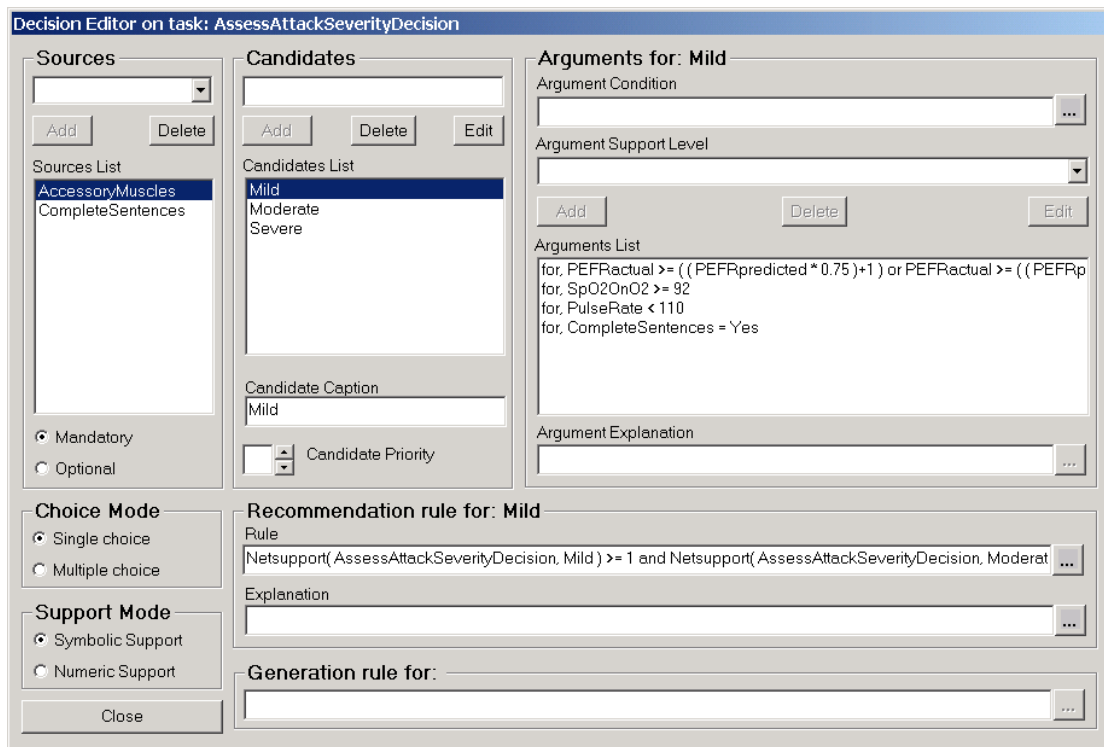
The Enquiry Editor allows data items to be added to Enquiry tasks. Clicking twice on the relevant Enquiry task icon in the Plans area opens the Editor. It contains a dropdown list box of all the data items that exist within the currently open guideline. The author selects the appropriate data item/s to add to the Enquiry task:



New data items are created with the Enquiry Editor.

### 3.5.2 Decision Editor

The Decision Editor is opened by clicking twice on a Decision task in the Plans area. The Editor is then used to create decision options, known as ‘candidates’, the arguments for and against each option and also to specify other decision attributes.



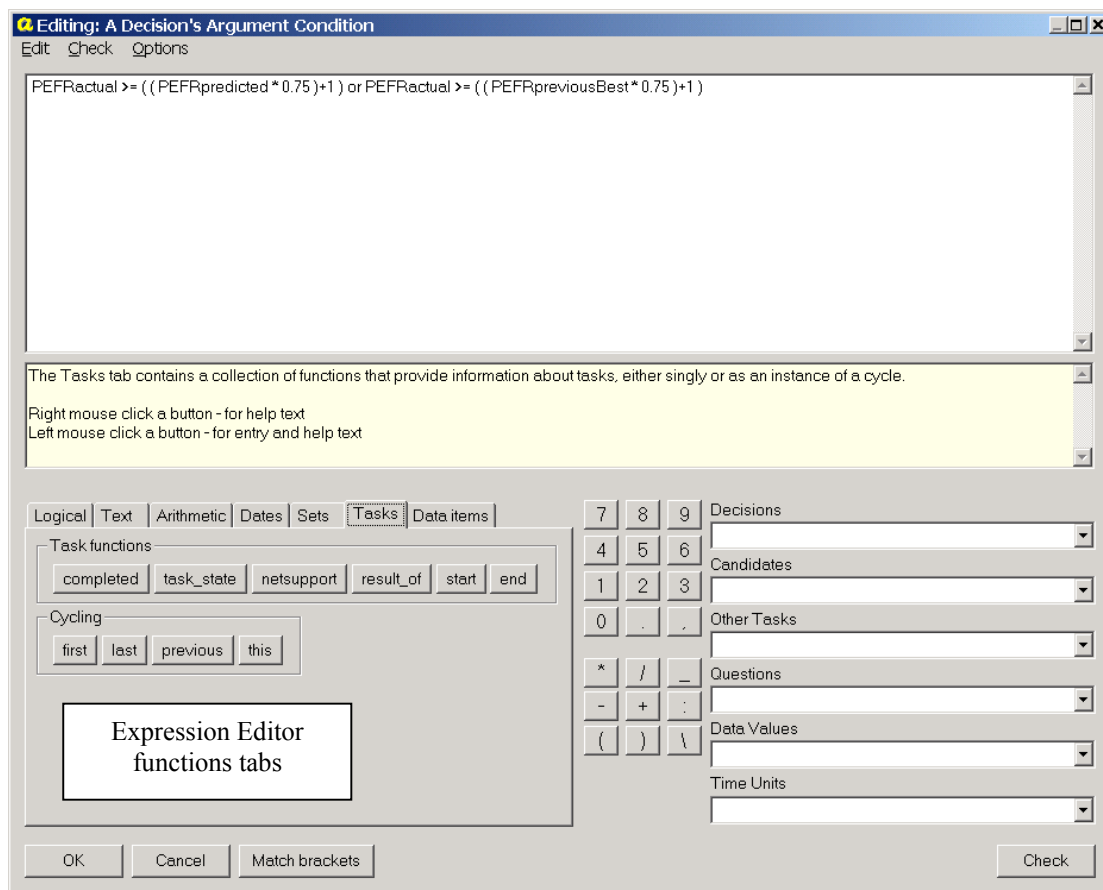
In the example above, the Decision task is designed to assess the severity of an acute asthma attack. There are three options: Mild, Moderate and Severe. The Arguments List refers to the Arezzo® arguments that are ‘for’ the ‘Mild’ option.

### 3.5.3 Expression Editor

The Expression Editor is a powerful tool that enables an author to create and amend Arezzo® **conditions** and **expressions**:

- An **expression** represents a value, which may be:
  - A number, data reference or date/time value for example
  - An arithmetic expression
  - A temporal expression involving temporal terms and temporal operators
  - A conditional expression involving ‘if’
- A **condition** is a term that contains at least one comparison operator. A condition evaluates to either **true** or **false**.

Below is an example of a condition that evaluates the patient’s current peak expiratory flow rate (PEFR) by comparing it with the predicted and previous best PEFR:



If this expression is true, then the relevant argument ‘for’ the option ‘Mild’ asthma severity will be activated.

The Expression Editor provides access to the extensive range of Arezzo® **terms**, which are data representations and operators used to construct complex expressions and conditions:

- Data items may have multiple values, which may either be manipulated as a set of values, or manipulated individually by specifying temporal aspects of the data. For example, a set of blood pressure values may have been recorded on several occasions. The functions ‘**first**’, ‘**last**’, ‘**previous**’, and ‘**this**’ would evaluate the appropriate data values in this set.
- All the usual arithmetic operators are available, along with various functions such as sum, average, maximum and minimum.
- Temporal predicates are provided, together with representations for the start and finish times of tasks, the current date and time, and the timestamps of individual data items.
- There are various comparison operators for comparing terms, and also the logical operators *and*, *or* and *not* for combining conditions.

In addition to Arezzo® terms, all of the task names, decisions, decision options (candidates), data items (questions) and data values are available to the Expression Editor, which significantly speeds up guideline authoring.

### 3.5.3.1 Temporal terms and functions

A powerful feature of Arezzo® is the capacity to represent date and time information in conditions and expressions. **Temporal terms** include:

1. **Absolute date/time terms** – either a date, time or a combination of the two.
2. **Time qualified data** – Every piece of data that is entered during guideline enactment has a timestamp. The default timestamp is the date and time at which the data was added to Arezzo, although the user may set the timestamp to the date and time the data was collected/recorded etc. A time-qualified data item would take the form “DataItem during Int” or “DataItem before T” where T is a time point and Int is an interval.
3. **Interval** – is the period between two time points
4. **Time points** – are represented in terms of **time events** and **time units**.
5. **Time events** – include absolute dates/times or the start and finish times of tasks
6. **Time units** – comprise an integer value and a unit measure of seconds, minutes, hours, days, weeks, months, or years.

**Temporal functions** include:

1. **datediff** – difference between two dates, which is specified in time units
2. **dateof** – the date when a data value was entered
3. **isafter** – a condition that is true if a datetime is after another datetime
4. **isduring** – a condition that is true if a datetime occurs within a time interval

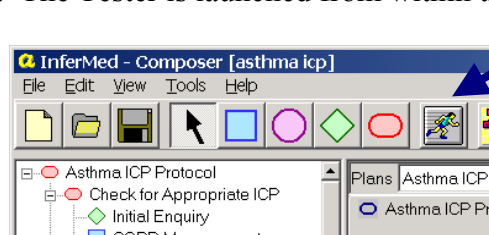
### 3.5.4 Arezzo® Class Editor (ACE)

ACE enables authors to create or load an external source of data items and data values, such as an ontology of clinical terms and codes. The Expression Editor can use these data items and values for creating Arezzo® expressions, as well as task names and decision option names. This tool facilitates the linkage between Arezzo® guidelines and electronic medical record systems.

## 4. What is Arezzo® Tester?

The Tester is an environment for testing guideline enactment. Once a guideline has been developed in the Composer, it may be enacted. This will demonstrate how a guideline will appear when run for a particular patient.

The Tester environment is not intended for clinical use: it is intended for testing and debugging the logic of a developed guideline. The Tester is launched from within the Composer:



## 5. What is Arezzo® Performer?

Arezzo® Performer is an inference engine that has been built for optimal speed and efficiency. The engine has a Microsoft COM layer with a documented API. This enables external applications to interface directly with the COM object.

At run-time, the inference engine loads the appropriate Arezzo® guideline. The various tasks represented within the guideline are processed. Every time a guideline is processed, the inference engine generates and maintains a state file, which includes a date/time stamped record of all data entered, decisions taken, and actions implemented by the user. Each individual state file can be stored electronically and reloaded into the Arezzo® inference engine, along with the parent guideline, to resume the individualised patient-specific guideline or care pathway instance.

The state file also serves as a detailed audit trail.

Currently, the inference engine is only available for WinTel platforms. A Unix-compliant version is under development.

## 6. InferMed's track record in Decision Support

*InferMed* ([www.infermed.com](http://www.infermed.com)) is a London-based UK company developing software for clinical research and healthcare. Originally a joint venture between a UK software company, and Imperial Cancer Research, now Cancer Research UK (CRUK) Europe's largest, research-based cancer charity, *InferMed* is now privately held, with CRUK a significant shareholder.

*InferMed* has used Arezzo® in a number of clinical decision support systems. Early Referral Application (ERA) (Larkin, Lancet Oncology, 2001) was a UK National Health System pilot project based on national cancer referral guidelines, to ensure that patients who require urgent referral, receive appointments within two weeks. ERA successfully demonstrated embedding of evidence-based decision support within an existing family physician system, (EMIS) and booking of appointments directly with the hospital. A particular strength is the minimisation of the number of forms and questions that the GP has to fill in to arrive at a recommendation.

Retrogram™ assists in prescribing of drugs for treatment of HIV infected patients. It uses data about specific changes in the viral genome present in the AIDS virus to evaluate the clinical utility of all appropriate drugs, and recommend treatment options specific to that patient's situation. RetroGram is in use by some 250 physicians worldwide and formal clinical evaluation showed that RetroGram(tm) improves the virological outcome when used in the resistance management of HIV-1 infected patients (Tural et al, AIDS, 2002).

Scientific evaluations of Arezzo® have also demonstrated improved family physician prescribing (Walton et al, BMJ, 1997) and genetic risk assessment of familial cancers (Emery et al, BMJ, 2000)

Arezzo® has been selected for use in three countries. In New Zealand, *InferMed* is working with the Best Practice Advocacy Centre, based in Dunedin. Guidelines are being developed for general practitioners. The guidelines are integrated with electronic patient records. In the Basque Region, guidelines for asthma are being used in hospital clinics. This work has been carried out by Basque University, in collaboration with *InferMed*. Wider deployment is planned. In Denmark, Arezzo® is being used by the Guidelines Development Task Group in the E:S Hospitals EMR programme. The first trials will get under way in March 2006.

Arezzo® is providing the decision support capability for the EU-funded COCOON Project (<http://www.cocoon-health.com/>). A variety of guidelines, including hypertension, chest pain, Parkinson's disease, diabetes and breast cancer screening, are being tested in the Lombardy, Epirus and Brussels Health Regions. In Lombardy, the guidelines are integrated with the general practitioners' electronic medical record systems.

Arezzo® will be providing decision support for the EU-funded @neurIST Project, which began on January 1<sup>st</sup> 2006 (<http://www.aneurist.org>). The aim is to provide specialists and GPs with a risk assessment and treatment planning tool for managing asymptomatic cerebral aneurysms.

InferMed, Brown University (Providence, RI) and Quality Partners of Rhode Island are collaborating on the MAPS Project. This project is delivering pain management guidelines into US nursing homes in Rhode Island. Nurses are using PDA devices to assess patients with chronic pain. Arezzo® provides recommendations about optimal pain management, as well as detecting clinical significant problems and providing alerts. Quality Partners are evaluating the use of the guidelines and the outcomes.

## **7. Conclusion**

Arezzo® provides a powerful solution to the problem of creating and running clinical guidelines and care protocols. The Composer enables authors to quickly create guidelines based on collections of generic task types. A variety of tools are provided to ensure that guidelines can be personalised to individual patients. The Tester is used to test the guideline logic before deployment. The Performer inference engine enables guideline enactment, with customisation to each patient.

Arezzo® technology has been evaluated in a wide range of applications in a variety of clinical settings in addition to those cited above, and has demonstrated its ability to provide support for the most complex guidelines.

Although designed to meet the needs of clinicians Arezzo®'s generic approach to decision-making and guideline development would be suitable for complex, value-laden decision-making in many other businesses.