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FIA Ref: Eng Man DRT1-6 PTM 100713

OPERATING MANUAL FOR CHEWING APPARATUS

DRT1 - DRT6
and
PTM models

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1. MANUFACTURER AND SUPPORT

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Answers to Frequently Asked Questions may be found on:
http://www.fia.se/english/faq.html

2. RANGE OF APPLICATION

The Apparatus is made to masticate chewing gums, especially medicated chewing gums. Other use is not recommended without a preceeding discussion with the manufacturer.

3. EQUIPMENT / CONSTRUCTION

The most important parts of the chewing apparatus are as follows:

Revolving device for the upper chewing surface
Stand
Thermostatted test cell
Upper chewing surface (upper jaw)
Lower chewing surface (lower jaw)
Device for axial up and down chewing motion
Lift
See Fig 1.

Electronic control device for chewing frequency, chewing time etc.
See Fig 2.

Mobile carrier
Water bath
See Fig 3.

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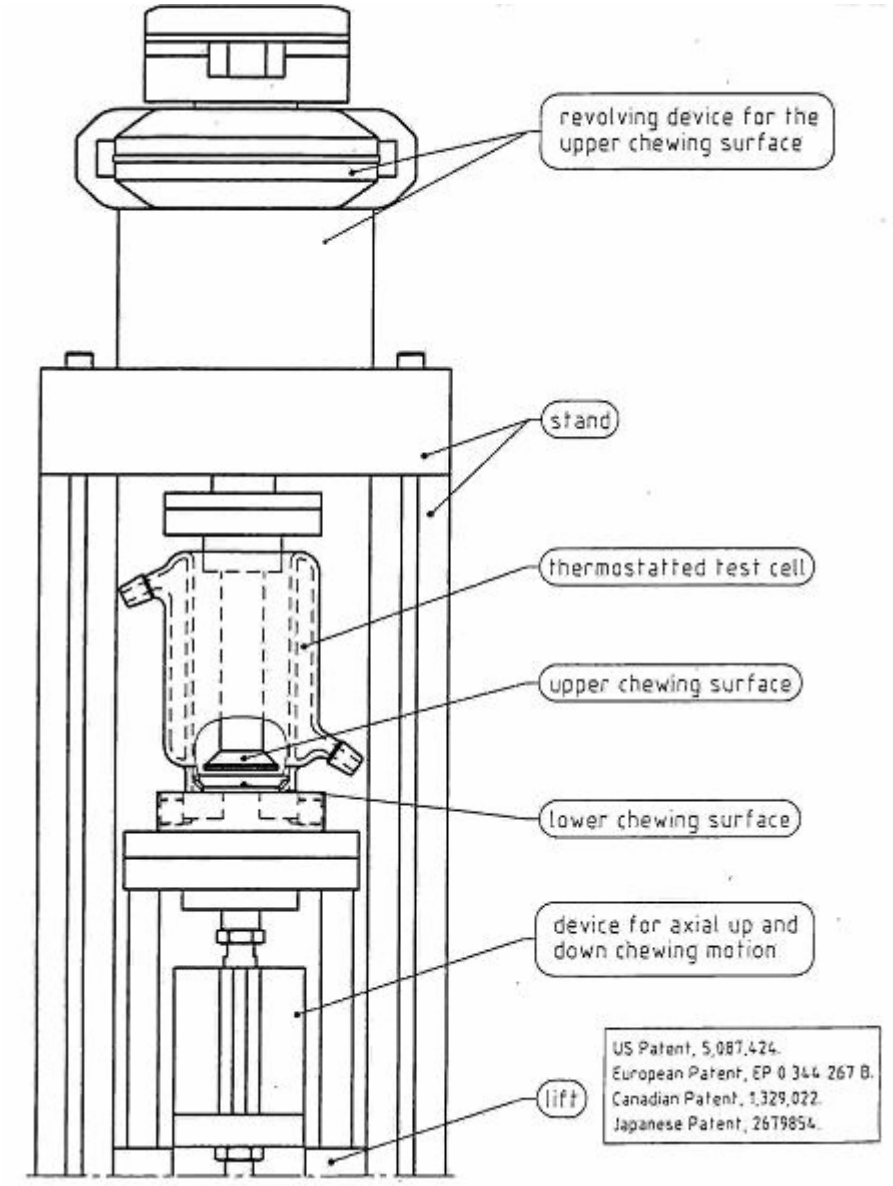

FIG 1. CHEWING APPARATUS: Chewing module.

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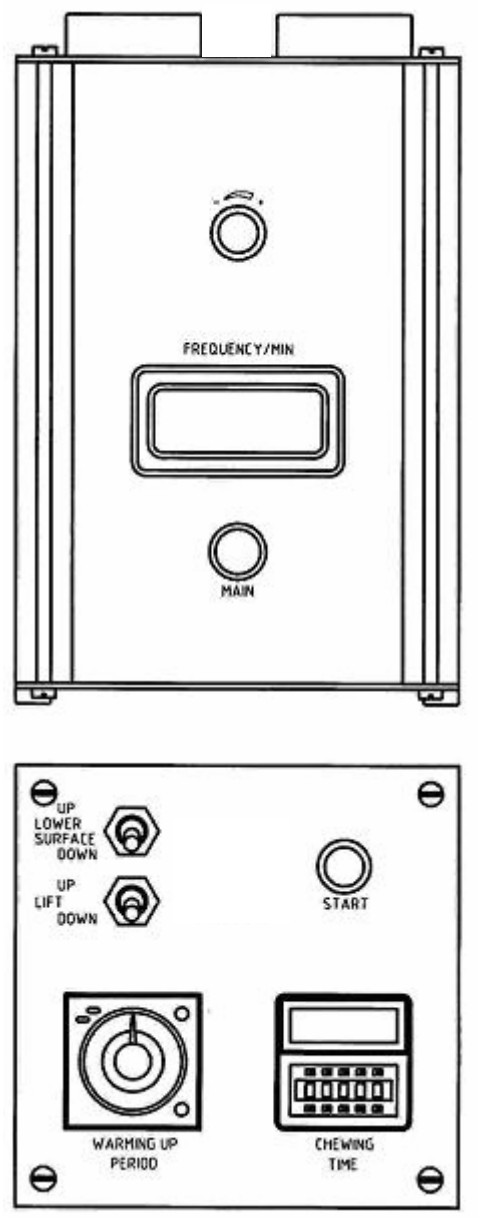

FIG 2. CHEWING APPARATUS: Electronic control device for chewing frequency, chewing time etc.

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The chewing equipment is placed on a mobile carrier. See Fig 3.

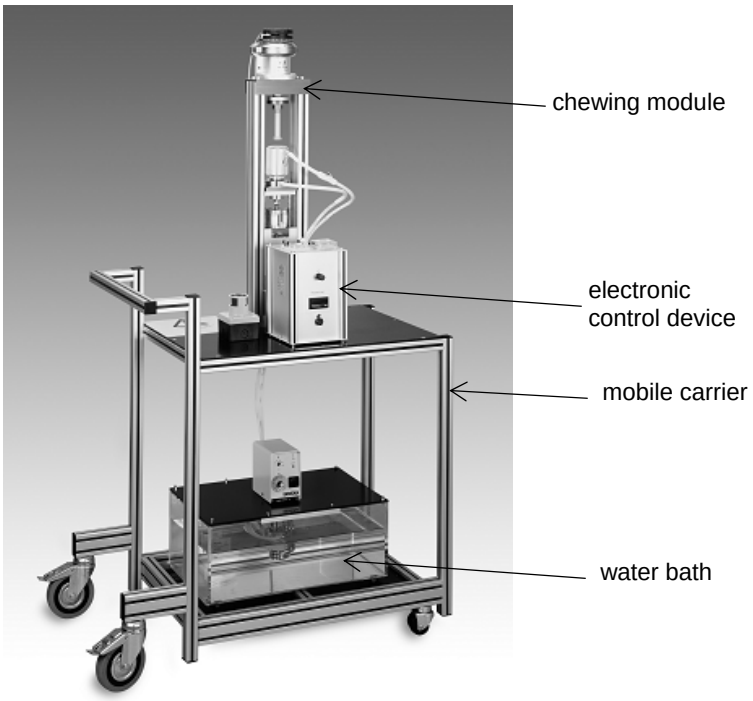

FIG 3. CHEWING APPARATUS: 1-cells equipment.

The material and the form of the parts that are in contact with the chewing gum are decisive for the function of the apparatus.
The material of the jaws is acid proof stainless steel with a blasted surface. The blasted surface makes the jaws get a good grip of the chewing gum during the mastication.
The upper jaw is stationary in relation to the lower jaw and also completely fixed against up and down going movements although it is turning around its axis by a revolving device. The lower jaw is moving up and down by a device for linear/axial chewing movements but is fixed against revolving movements.
The test cell follows the lower jaw in its movements.
The chewing procedure consists of up and down going strokes of the lower jaw in combination with a shearing (twisting) movement of the upper jaw which provides a mastication of the chewing gum and at the same time an adequate agitation of the test medium.
It is possible to raise and lower the unit ”lower jaw / test cell” by an lift device. If you lower it to down position it becomes competely freestanding from the upper jaw which facilitates the preparations for analysis, for sampling, for emptying and

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cleaning after analysis. During sampling the mechanical processing and the stirring stops which means that also the release of drug stops.
The upper jaw has an flat underside which is parallell to the central part of the lower jaw. The small brim of the lower jaw is angled upwards (45 degrees) so that the lower jaw fashions a small bowl with flat bottom. This bowl prevents the chewing gum from sliding during mastication. It can be of advantage to use circular nets of inert polymer to keep the chewing gum in place between the jaws during the analysis.
The thermostatted test cell is made of glass and is transparent which allows visual inspection during test.
The thermostatting is complemented with a thermostate chamber of metal which is in thermal contact with the lower jaw. The upper jaw is not heated and is attached to a heat insulating axis.
The water bath is to be filled with of deionized water and is heated by a circulation heater. (See also the operating manual for the heater).

3.1. VARIETIES AND OPTIONS

The chewing apparatus may have between 1 and 6 chewing modules or cells.
A safety cupboard is mounted on all varieties produced from 2005 and on. See Fig 4.

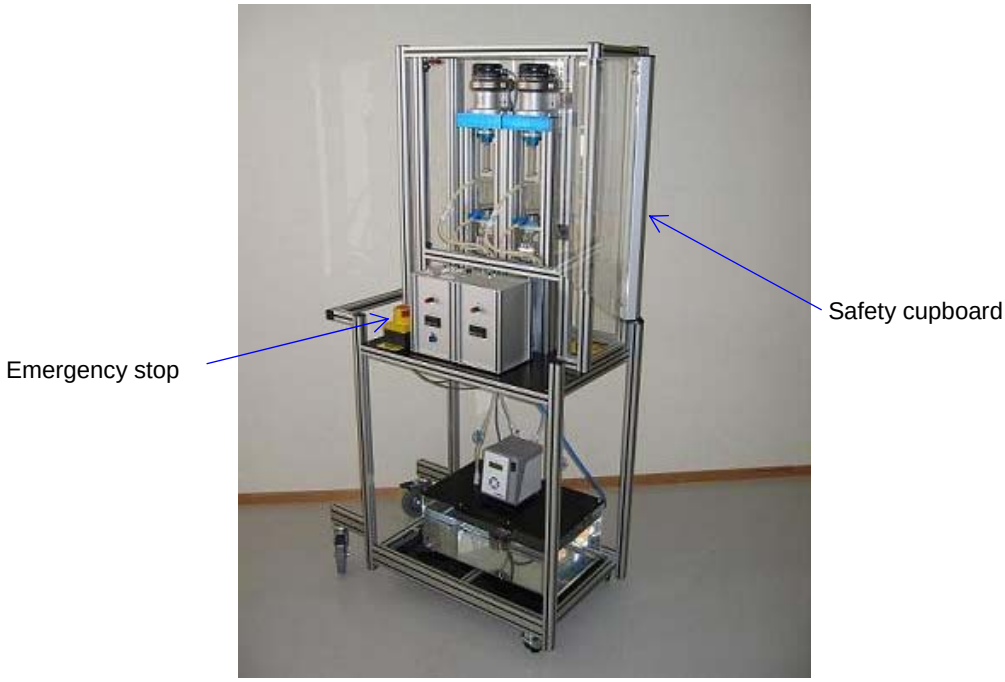

FIG 4. CHEWING APPARATUS: Safety cupboard.

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When the door to the safety cupboard is opened, the power is cut to the control unit and the compressed air is shut off. The action is the same as for the emergency stop (see below). The pneumatic cylinders are blocked if they are in their upper positions. It helps to adjust the gap between jaws since the door is opened during this procedure. See section 7.1.3.

3.2. SPECIFICATIONS FOR SUPPLY, DIMENSIONS

Voltage:	230 VAC, 1000 to 2300 VA(W) depending of heater type (optional: 115 VAC).
Compressed air:	6-8 bar (85-110 psi), minimum 20, 40 or 60 l/min is needed for 1,2 or 3 cells varieties of the Chewing Apparatus. 100 l/min for 6 cell models.
Dimensions:	1645 x 660 x 510 mm HxBxD (1-3 cells). 1645 x 1380 x 660 mm HxBxD for the 6 cell models.
Weight:	30 - 40 kg (1-3 cells). 80 kg for the 6 cell models.

4. EMERGENCY STOP AND SAFETY

The equipment must be handled only by personnel trained on the apparatus. The training must include handling of the emergency stop.
The emergency stop is placed by the main control unit. See Fig 4.
While the emergency stop is pressed down the power to all units shut down and at the same time the supply of compressed air to all pneumatic cylinders is shut. The door of the cupboard is connected with the emergency stop by a safety switch and opening of the door has the same effect as pressing the emergency stop. This effect must never be set out of function. If by some reason the safety switch at the door fails or is set out of function, it is prohibited to use the chewing apparatus. Only specially trained service personnel should remove the rear acrylic glass plate of the shelf for service purposes. The shelf must always be undamaged and complete to avoid clamping risk.

5. METHOD

All the adjustable parameters that are described in this manual including the chemical compositions of the dissolution medium are specified in different Methods (described by the user company in the applied analytical methods for the actual chewing gum that is tested). Please note that all adjustable parameters may be specific for each individual formulation.

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6. HANDLING

6.1. PREPARATIONS

Some basic parameters are preset like temperature, gap between jaws, frequency and angle of rotation. See 7.1 ADJUSTMENTS to change these parameters.

On the control units, put the switches like follows:
LOWER SURFACE = **DOWN**
LIFT = **DOWN**

Check that the power is off (the botton MAIN). A lamp indicates power on/off.
Open the door of the cupboard.

On the center of the lower jaw´s base chambers you shall put o-rings. The o-rings must be clean and shiny. They should be treated with a small amount of vacuum grease or silicone oil and wiped off with a cleansing tissue, close to dryness.

The lower and upper chewing surfaces are mounted by clockwise rotation, fingertight. Please note that clockwise rotation of the upper surface is applied while viewing the jaw from underneath. No tools are used during mounting. The o-ring is surrounding the lower surface.

Connect glass cuvettes to the quick couplings and mount them by a slight clockwise rotating movement, firmly but carefully, pressing them over the o-rings on the lower jaw. If the o-rings are properly pretreated, the mounting is smoothly and the cuvettes stand in an upright position without any tendency to slip off the o-rings unprovokedly.

6.2. STARTING

Fill up the cuvettes with liquid according to method.

Put the chewing gums in place in the cells and eventually support nets according to method.

Close the door of the cupboard.

On the main control unit:

Turn the power on by pressing the botton MAIN. A lamp indicates power on/off

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WARMING UP PERIOD: Put the time to 10 min or else according to the method. (Mode A on the timer is always chosen and the display 0-30 min).

CHEWING TIME: Put the time to the event for the first sampling.
(the letter **C** should be displayed on the left of the digits, exept for the PTM-models where an **A** is displayed. On the right, an **m** is displayed, standing for minutes).
On the control units put the switches:
LIFT = **UP**

Note: CLAMPING RISK!
The lifts moves the lower jaws with the glass cuvettes against the upper jaws with a considerable force (about 500 N). The safety cupboard is there to protect the operator.

Press START firmly once for about a second and a green lamp on the timer for WARMING UP PERIOD flickers and indicates that its counting down the preset time after which the chewing procedure starts.

6.3. SAMPLING

The chewing stops automatically at the preset time for the first sampling.

On the control units put the switches:
LIFT = **DOWN**
Open the door and take out samples from the liquid (mix the liquid before sampling).
Close the door.

Change CHEWING TIME to the event for the next sampling (the time difference between previous and next sampling).
Set WARMING UP PERIOD to 0 (zero).

On the control units, put the switches:
LIFT = **UP**

Press START and continue the experiment.

6.4. TERMINATION

Check that the lift is in down position. Turn off power and compressed air.

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6.5. EMPTYING

The cuvettes are emptied with vacuum to waste or with a syringe. They are removed from the equipment. Remove nets and gum remains. Wipe off all remaining liquid with a paper cloth. After that the jaws are removed. Any drops of liquid are again wiped off the instrument parts.
The cuvettes are cleaned (washed off with deionized water) and the used jaws are collected for cleaning service. Fresh qualified jaws are used for the next analysis. (See 7.2.2. The cleaning of the jaws).
If the jaws are stuck and difficult to remove with your fingers, use primarily a dry paper cloth to get a better grip. Stuck jaws may occur on new chewing apparatus or with new jaws. Inspect the threads and remove any burr or gum remains. Never use an unprotected steel gripper on the jaws. A special gripper with aluminium lining is available.

7. MAINTENANCE INSTRUCTIONS

7.1 ADJUSTMENTS

The most important parameters which effects the release of drugs are adjustable. Ajustments are normally not necessary if one and the same formulation is tested repeatedly.
Adjustments may be necessary to make before the tests on another gum formulation.

7.1.1. Temperature

The temperature can be set in the interval 25 - 45 °C. The adjustment is made by the thermostat of the water bath (see separate manual). The temperature is set slightly higher than the desired temperature of the dissolution medium in the test cell (0.3 to 0.5 °C higher). This is to compensate the cooling of the test cell by the surrounding air.
The dissolution rate is generally very sensible to the temperature. Cold gums becomes also hard and may be impossible to masticate with the standard chewing apparatus (see Appendix 1 about PTM-models).

7.1.2. Time

There are two timers on the control device (see **FIG 2**). WARMING UP PERIOD regulates the time before the chewing has started CHEWING TIME is used for adjusting the mastication.

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Example:
WARMING UP PERIOD is normally put to between 5 and 10 minutes to make the temperature of the dissolution medium come to balance before the chewing is being started.
For example, CHEWING TIME is put to 2 minutes. The experiment then starts with a 5 min pause before the 2 min period of mastication. The operator is able to leave the apparatus for a while and then come back: lower the lift, open the door, take a sample, raise the lift, put WARMING UP PERIOD to zero, CHEWING TIME to for example 3 minutes, then start again – wait, make the next sampling, … .
Dissolution takes place only during the mastication. If the equipment is left while the operator takes a break, it does not effect the dissolution performance.

7.1.3. Gap between jaws

The gap between the jaws (when they are closed – chewing position) is adjustable between 0 and 10 mm. The factory setting is about 1.6 mm.The adjustment is made by removing the test cell, placing a blank (not blasted) upper jaw on top and a blank upper jaw in the bottom. See **FIG 5**.

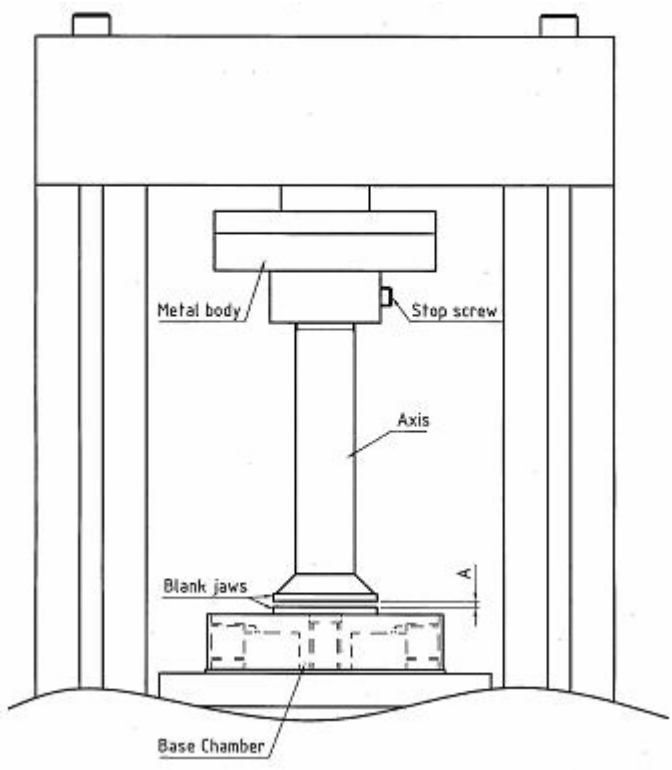

FIG 5. CHEWING APPARATUS: Gap between jaws.

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On the main control unit (and the door closed):

Turn the power on by pressing the botton MAIN. A lamp indicates power on. LIFT **and** LOWER SURFACE is put to **UP** position, which means that the lower jaw is in its highest chewing position.

Open the door.

With a thickness gauge the distance is set by loosening the stop screw* on the metal body (upper jaw), hold around the body and screw the axis to correct distance. Then the stop screw is fastened (twisting moment 1±0.2 Nm) with a hexagonal key.

Leave the switches on the control unit like they are.

Close the door.

* Models fabricated from July 2010 and later will not have any stop screw but a locking ring for fixation of the axis. It is sufficient to fasten the locking ring finger tight and the axis will be fixed in position. See Fig 5B.

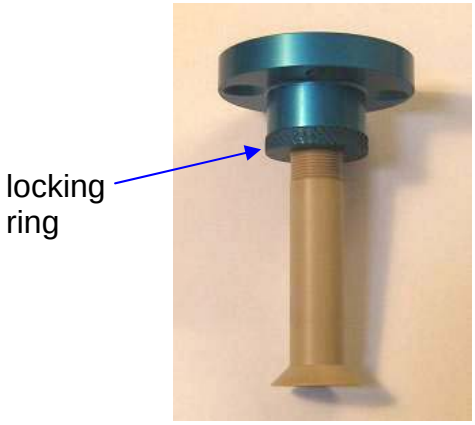

Fig 5B. Axis with locking ring.

7.1.4. Frequency

The supplier has preset the maximum chewing frequency and locked it at approximately 64 strokes per minute (at a pressure of 6 bar).

The obtained chewing frequency can be read during ”Chewing” on a frequency counter, a display on the control device. The display is updated twice each minute. Average value is observed during some minutes to get a representative figure. Normally the frequency is set before an experiment is started or at least checked during some minutes. This may be made with or without glass cuvettes mounted.

The relevant frequency for a certain analysis is adjusted by the operator using the knob on the driving unit. Each cells frequency may be adjusted individually. The obtained frequency may be read on a display on each cells control unit. To obtain a representative value on the display the apparatus must work for at least half a minute after adjustments.

Adjustments can be made in the range of about 15 to 62 cycles per minute.

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7.1.5. Angle of rotation

The angle of the turning motion is adjustable in the interval 10 – 180 degrees. The factory setting is 20 degrees.
Adjustments of the angle is made as follows. See **FIG 6**.

FIG 6. CHEWING APPARATUS: Setting the angle of rotation.

Disconnect the compressed air and let the pressure out. Loosen the socket head cap screw with a hexagonal key. Set the turning angle. Move the stop knob to its stop. Tighten the socket head cap screw again with a hexagonal key (3 Nm).
The procedure can be repeated with the other stop knob; it is the difference of angle between the two which gives the total turning angle.

7.1.6. Volume

The test cell can be filled to a volume of 20 to 70 ml of dissolution medium which means ”sink condition” for release by most of the common drugs which are administered by medicated chewing gums. The volume admits repetetive sampling without disturbing the release. Special cuvettes, operating with an external sink are available for sparingly soluble substances.

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7.2. SERVICE

7.2.1. Current Service

Current service is performed on daily or weekly basis according to regulation in SOP and checkpoints includes:

Cleaning
Cursory cleaning.

Gap between jaws
See above under Adjustments

Frequence stability
A preset frequency should not change from day to day by more than 2 strokes/min up or down. Observations are made on the displays.

Temperature stability in water bath
The preset temperature of the water bath must not change from day to day. Observations are made on the display.

Temperature obtained in cuvettes after WARMING UP PERIOD
The temperature must be the same in all cuvettes after the WARMING UP PERIOD and must be in accordance with the method. Measurements are made on the dissolution medium with a calibrated thermometer. See also above under Ajustments.

Even and liberal flow through cells
Check that no knees or constraints appear on the tubing. The reflux from all six cells back into the waterbath should be evenly distributed and with liberal flow.

Liquid leakage
No leakage is accepted

Compressed air pressure
The pressure level of compressed air should be even and set to about 6 bars (84 PSI) during normal operation. Changes greater than 0.5 bar up or down during an ongoing experiment might have effects on the frequence stability. Pressure under 4 bar might have effect on the mastication procedure.

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Compressed air leakage
No detectable leakage should be accepted while using leak detection liquid (ie soap water).

Visual damages
Visual damages are to be reported and damaged parts if necessary to be replaced with spare parts.

Deviations from normal operation
Observations are made continually to detect deviations from normal operation at an early stage. Deviations are recorded in a loggbook and if necessary reported to the supplier.

7.2.2. The cleaning of the jaws

In every analysis which may take place many times per day, the cleaning of the jaws before analysis is as important as weighing, preparation of dissolution medium and correct final analysis.
The test cell is easy to remove and clean. The jaws are also easy to remove and switch to clean ones (see HANDLING: Preparations). Cleaning service of jaws and qualification of the jaws is normally performed by the supplier.
The procedure is all the same described below.

Rinsing (recommendation):
Unclean jaws with chewing gum remains is put in waterfree acetone and then cooled in a freezer to - 20 °C. Then they are put in a powerful ultrasonic bath for 3 minutes whereafter they must be brushed with a nylon brush to remove chewing gum remains while they are still cold (-10 °C). Sonicate in acetone (pro analysi) for 3 minutes. Now each individual jaw must be dried and inspected. After this it's time for blasting (according to recommended method) and again sonicate in distilled water for 3 minutes and wipe off each individual jaw on the back side with a clean paper tissue. Finally in acetone (pro analysi) for 3 minutes. To finish dry each individual jaw.

Blasting (recommendation):
Sand blasting is performed in a blaster that may not be used for any other purposes than for the treatment of jaws. Any contamination of foreign material could be harmful to the surface or the quality of the jaws.
Blasting must be included in every cleaning before use.
The blasting is made in a room seperated from the laboratory.
Example of method: Use a blasterpistol ANI (or equal) with inner orfice 3 mm and outlet 6 – 10 mm. The blasting is done during 3 – 5 bar with an distance of 5 – 20

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cm and with a rotating movement covering the whole surface of the jaw during about 1 minute. The blaster sand consists of aluminium oxide 0.2 – 0.4 mm, 5 -10 kg per batch. Minimum 10%, normally all of the sand must be changed after each batch of 120 jaws.

Inspection (recommendation):
Measure the thickness on the flat part of the jaw using a micrometer or 3 decimal instrument for thickness measurements. This must be done on all jaws before blasting.
The requirements that the thickness should be 2 ±0.05 mm must be performed. Jaws that don't fulfill the requirements are disqualified.
After blasting and sonication, the surface roughness must be measured and should be between RA 1.8 and 2.3 unless another value is specified in the analytical method. The sampling is made three times on each 10:th jaw. The whole batch of jaws that doesn't fulfill the requirements is disqualified.

7.2.3. Half Year service

Documentation of chewing sequences (frequences)

Eventual adjustments (visual check)
(settings are normally checked and if needed, adjusted while making Annual service)
-Movement intervals
-Levels
-Calibrations

Control of settings
-The centering an parallellism of chewing surfaces
-The frequency span
-Veryfying real frequence
-Veryfying that the temperature of the water bath is correct
-Control of the water bath (vibrations, dissonance)
-Veryfying that the timers are correct
-Control of the stand (fixtures and screws)

Cleaning
Algae and other microorganisms grow normally in the waterbath and the varm water circulation in the cuvettes and tubing. It is necessary to clean the waterbath every now and then. Tubing and cuvettes should normally only have to be changed or purified once per year. See Annual Service.

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7.2.4. Annual Service

Annual service includes besides the Half Year Service:

Tubing
Change of all tubings, sockets and connections

Cleaning
Thorough cleaning including washing inside of cuvettes and internal parts of water bath

Frequency
The maximum chewing frequency may be changed by adjusting four different valves for compressed air on each unit. This should only be done by the supplier or by trained personell. The maximum frequency is set at the factory to about 56/min.The valves control also the speed of the chewing movements, see **FIG 7**.

A chewing cycle consists of four movements:
1) an up going movement (PRESS), 2) a revolving motion forward (TWIST), 3) a down going movement (OPEN) and 4) a pause when the revolving device ”reloads” (REGAIN).
Normally the intention is to distribute the time for each mastication movement equally over the chewing cycle in releation their linear or periferial speed. During Regain (the pause) no mastication takes place, only a pause for drug release at the freshly exposed surface. The Twist operation is given the same time as the linear movements, Press and Open, together. Regain is given the same time as Twist.

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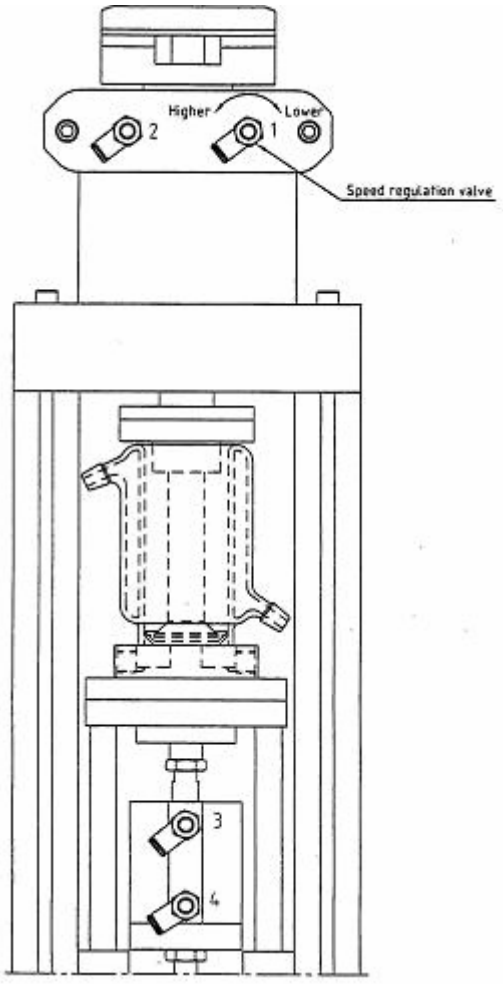

FIG 7. CHEWING APPARATUS: setting maximum chewing frequency.

The operation of adjustments is a bit tricky. Please contact your supplier if any doubt of how to handle the situation.
The procedure is all the same described below:

Recording
Recordings are made by a special instrument, designed for this purpose, or with an oscilloscope.
The rear (older than 2008 models) or the front panel of each electrical control device has got a nine pin D-sub female connector with the following pin designation:

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1. + 24 VDC
2. - 24 VCD (common)
3. (+ 24 VDC) signal lower position of lower jaw
4. (+ 24 VDC) signal upper position of lower jaw
5. (+ 24 VDC) signal 0 degrees turn of upper jaw
6. (+ 24 VDC) signal full turn of upper jaw
7-9. Not Connected

Signals from pins 3-6 are recorded with 2 (common) as reference for each chewing cell.

Measuring

Measurements are made and the durance of each of the four movements are calculated in milliseconds. The special instrument will give these values directly on the display.

Evaluating

Evaluation of the measurements are made keeping in mind the following scedule:
Up going movement of the lower jaw takes place while the sensor for the 0 degrees turn of upper jaw gives signal (pin 5).
Revolving motion forward takes place while the sensor for the upper position of the lower jaw gives signal (pin 4).
Down going movement of the lower jaw takes place while the sensor for full turn of the upper jaw gives signal (pin 6).
The revolving device reloads while the sensor for the lower position of the lower jaw gives signal (pin 3).

Adjusting

Adjustments on the individual chewing movements may be made using the four speed regulation valves on each cell of the chewing apparatus. See **FIG 7**.

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8. TROUBLESHOOTING

8.1. UNSUFFICIENT SUPPLY OF COMPRESSED AIR

Some frequent occuring problems after installation in a new site or in a new place in the laboratory depend from unsuifficient supply of comressed air.
Symptoms may be that the maximum chewing frequency is not reached for all cells. Some cells may even stop chewing. A clear indication of unsuifficient supply is that one or more cells may work in a correct manner if the other cells are blocked. (Blocking of a cell may for instance be accomplished by putting the switch LOWER SURFACE in position UP). Minimum air flow for six cells is recommended to 100 liters per minute supply of compressed air measured at 6 bars (84 psi).
Please note that no leakage of compressed air is accepted since it may affect the chewing frequency and chewing functions.

8.2. SENSOR FAULT

If all cells but one work properly but one is stopped check that the switch LOWER SURFACE is in it´s DOWN position.
If the cell still does not work check that the pressure on the compessed air is about 6 bar (84 psi), definitly not under 5 bar (70 psi).
If the device for axial up and down gowing chewing motion **FIG 1** (the pneumatic cylinder) is in it´s upper position the "lamp" (LED) of the sensor on the left side (seen from the front) must be lit indicating signal for upper position. If the device is in it´s lower position the sensor LED for lower position must be lit.
If you look at the revolving device for the upper jaw it has also got two sensors that signals 0 degrees turn or full turn. One LED must be lit also on the revolving device.
If there is a sensor fault it may be overcomed by moving the sensor position slightly (not more than 1 mm in any direction). This operation of adjustments is tricky and should be left to trained service personell. Please contact your supplier if any doubt of how to handle the situation.

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9. REFERENCES

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Apparatus for studying in vitro drug release from medicated chewing gums:
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International Journal of Pharmaceutics, 189 (1999) 57-65.

This link is for Frequently Asked Questions: http://www.fia.se/faq.html

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Appendix 1: DRT-models with Pressure control and Torque Monitoring (PTM).

This is a brief introduction to a series of models of chewing apparatuses with extended possibilities for measurements. They may also be equipped with pH and temperature logging.

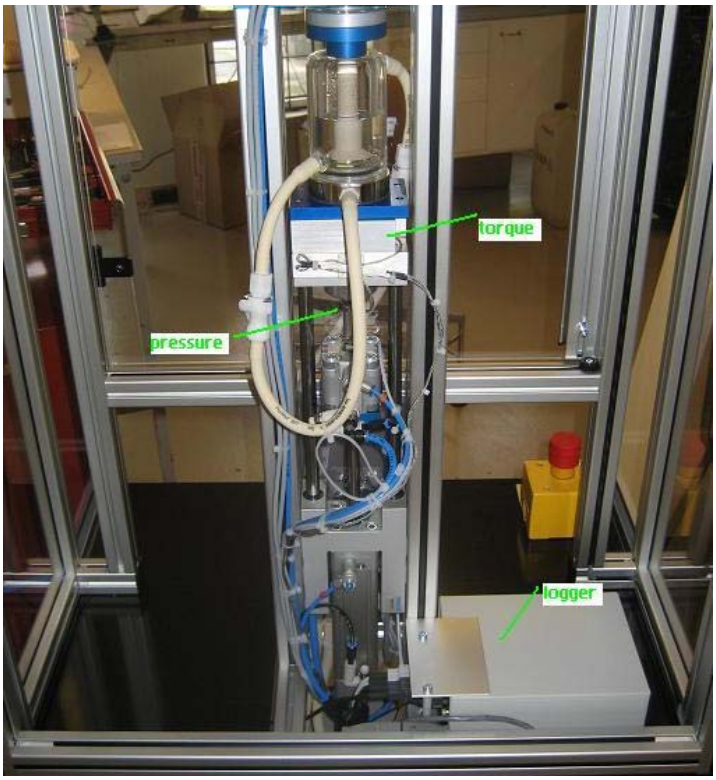

FIG 8. Chewing apparatus with load cells for pressure and torque measurments, PTM-models.

The photo shows the hardware of a Chewing Apparatus with exta hardware, namely torque and pressure sensors and data logger. The logger is connected to a computer with suitable software.

The standard Chewing Apparatus from FIA-Erweka DRT1-6 series has a fixed operation for the masticating jaw´s movements. The linear movements Press and Open are achieved by a pneumatic cylinder that is forced to reach the end positions of the cylinder. In a similar way the twist motion must always reach the end position (Twist).

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(The positions of the twist cylinder are Twist and Regain, where only Twist is acting on the chewing gum by torque forces).

Several of our customers have expressed interest in an ability to register pressure and torque forces during the mastication of chewing gums. Also the possibility to set a maximum pressure value has been of interest.

A problem has been that the preferred chewing frequency is normally about 40 cycles/min. Each cycle is divided in four movements; Press, Twist, Open and Regain. Press thus takes less than 300 milliseconds (ms) resulting in a measuring sampling speed of less than about 100 ms to be able to control the movement.

Recent developments of electronics now have made it possible to construct a chewing apparatus with both pressure control & monitoring and torque monitoring.

If the maximum value is reached, the twisting movement of the jaws is achieved even if the end position of the Press-movement is not reached. With a hard gum, the gap between the jaws must not necessarily be reached before Twist motion is applied on the gum.

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Appendix 2: Frequently Asked Questions

(about the chewing apparatus, chewing machine, dissolution rate tester, DRT)

Before buying:

Question:
Will FDA (Food and Drug Administration) accept a file with data from this instrument?

Answer:
Yes, they will. European Pharmacopea, EP have published it in the April issue of Pharmeuropea 2008 for submission. Apart form that, Nicorette and Rugby Nicotine gums are registered in all countries with dissolution data from this very Chewing Apparatus. It is spread throughout the world is now to be adopted in EP, US Pharmacopea etc. All experts agree that in vitro testing must be demanded also for Medical Chewing Gums and not only for other formulations like tablets etc. In EP a machine is described with poor specifications, no default settings or details. It is to some extent similar to the FIA / Erweka Chewing Apparatus, but many points differ.

Advantages with the FIA / Erweka Chewing Apparatus are:

- It is well known by FDA and other authorities worldwide
- Reproducible results with low standard deviations
- It is sized to fit the analytical laboratory and is silent
- It has transparent dissolution cells for good visibility
- Operating height in positions to achieve a comfortable working environment
- Easy to prepare and fast to reload and warm up for effective handling and use
- Well documented examples for use
- Easy to change settings of Chewing parameers
- Good support for method development

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Question:
How can we perform IQ / OQ (Instrument Qualification & Operation Qualification)?

Answer:
Normally this is done by the customer with minor support from the distributor. IQ / OQ documents for the chewing apparatus may be supplied by the distributor that also may help you with the tests.

After unpacking:

Question:
Will we get any further support with method development etc. ?

Answer:
You will get free expert support via e-mail (i@fia.se) as far as possible. You may also get support with method development including chemical analysis from our training and method development centers against payment. Please ask via e-mail for advice.

Questions about technical details:

(Some of the questions below are discussed in the manual. A good advice is to read it carefully before starting with any experiments).

Question:
How can we arrange supply of compressed air?

Answer:
In the manual you will find the demands. Many labs have compressed air connections in the building or in each lab-room. For a 6-cell Chewing Apparatus, compressed air of 6 bar (84 psi) and minimum 100 liter per minute is needed. Normally a standard compressor is placed in a room, separated from the lab and preferably sound insulated (the cellar). In the lab a permanent installation is made on the wall with a reduction valve and a manometer where the pressure may be read. A water trap is mounted at the reduction valve. All the items mentioned are standard and may be found in a machine or hardware store.
For a 1-cell Apparatus a large tube with compressed air may be used or a compressor of "Silent Air"-type installed in the laboratory. All models from 2007 and on have a suitable reduction valve with manometer and water trap mounted on the carrier.

Question:
What is the use of Support Nets ?

Answer:
Support nets are more or less compulsory to use. It may be worth a try to make chewing without nets but it is likely that the gum or pieces of it will try to creep out from the jaws

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during mastication if no nets are used to keep it together in a unit between the jaws. The nets are cheap and quite inert (from Nylon, PA).

Question:
How many pair of jaws do we need?

Answer:
It depends from how much you use the chewing apparatus. The idéa is that the operator simply put the used jaws to the side and replace them with a clean and qualified pair. This is a cost effective use of the chewing apparatus and the trained operators. This means that cleaning and qualification of the jaws has to be made batchwise. A batch should be of minimum two weeks use. One batch is cleaned and qulified while another batch is being used. So the need will be at least two batches.
We recommend for a 6-cell chewing apparatus 120 pair of jaws and 60 pair for a 1- or 2-cell apparatus. For a start, of course a smaller amount may be tried.

Question:
Where can we get Dissolution Calibrator Gums?

Answer:
We are optimistic about a calibrator to appear in the near future. So far we may only use samples of well known medical gums as reference material. On request we will suggest a suitable gum that is available in your own country.

Question:
How can you find out the correct gap between the jaws?

Answer:
The gap depends on the volume of the gum and a bit apon the formulation itself.
To find the correct setting is a trial and error issue.
The in vitro dissolution profile should be related in some way to the in vivo profile.
For instance; the final amount dissolved should be about the same level for in vitro as in vivo. A retarded in vivo profile should be reflected in a retarded in vitro profile etc.
Normally support nets are used (see above). A too narrow gap will often be reflected in a destruction of the nets (see Picture 1). A too wide gap will result in poor mastication, a lost grip on the chewing gum and a resulting false slow release (see Picture 2).

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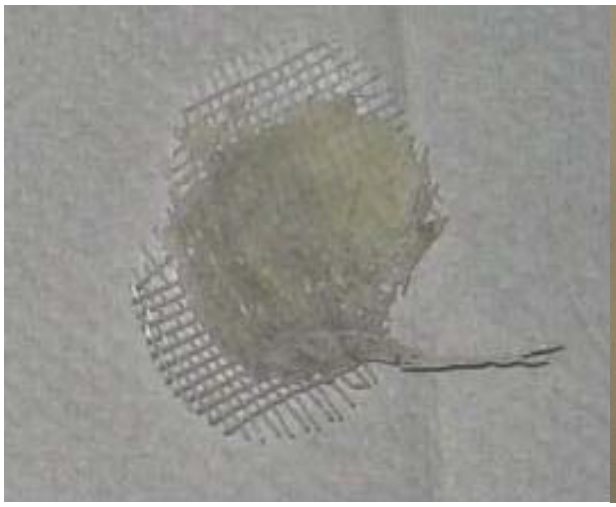

Picture 1: too narrow gap.

Picture 2: too wide gap.

When the gap is correct, the chewing gum is masticated well and often may remains be left on the lower jaw after the dissolution test(see Picture 3).

Picture 3: remains on lower jaw after well masticated Nicorette Mint 1.4 mm gap.

Question:
When jaws are stuck or difficult to remove, any tricks or tools?

Answer:

Try to use a piece of dry paper tissue; it should normally be possible to remove them with finger force. Never use a metal tool directly on them, tools have to be carefully

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covered with some soft tape or cloth. A special tool is available.

Question:
Which importance does has the Warming up Period have?

Answer:
The chewing gum is harder at room temperature than at the temperature where dissolution is performed. With some formulations it is not even possible to masticate the gum with the chewing apparatus at room temperature since the gum is too hard. The dissolution testing should normally be performed at constant temperature close to 37 degrees Celsius.
The Warming up Period is a waiting period for the chewing gum and the dissolution medium to stabilize and reach the constant temperature at which the dissolution testing will be performed. The gum, support nets, dissolution medium and the upper jaw are all temperated during this period. No dissolution from the contents in the gum base takes place before the mastication is started.
Warming up takes place only once, before actual dissolution testing starts. A typical value is 10 min. If the gum is coated, the coating will normally be partly or totally disintegrated during the warming up period, leaving the gum with the active substances exposed before the mastication starts. If the coating contains active substance, some special measures can make it possible to chew a cold gum. Please consult i@fia.se .

Question:
How is sampling made?

Answer:
Manual sampling is made after lowering the lift. Before sampling the dissolution medium is stirred or liquid are repeatedly withdrawn with a pipette and put back to obtain a uniformly mixed liquid.

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Picture 4. Liquid at the first sampling point, before mixing.

Sampling is normally made with a pipette (volumes up to about 1 ml). The sampling volume may be compensated with fresh dissolution medium, but this is not necessary. Calculations to compensate for successively decreasing volume of dissolution medium may be made done with the same mathematical methods as for normal tablet dissolution. After sampling, nets and gum are put in the center of the lower jaw. No dissolution takes place when the gum is not masticated. The time that the sampling takes is of no importance to the dissolution test.
Automatic sampling is possible but we have yet little experience about it. A special cuvette with sampling tube is used and samples are withdrawn for instance with a peristaltic pump. Prior to sampling, the liquid must be mixed to obtain a homogeneous solution.

Question:
The cuvettes are made of glass. Is there a risk of damage?

Answer:
With careful handling and with O-rings in good condition the cuvettes will last for many years without damages or other problems. The inside tube of the cuvettes is made from high precision glass thus having very exact measures. The O-rings must be original and

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having a clean surface, slightly shiny from silicone oil (compare Manual). Excess oil may cause that the cuvettes slips off. A surface with gum remains, may cause high friction and if the cuvettes are not put in position with a screwing clockwise motion, but pressed with force straight down, they may “jump” suddenly down to the metal surface and pieces of glass could be cracked off the lower surface of the cuvette. With correct handling, the change of jaws and restart of a new dissolution run is very fast and effective.

Question:
What about Service on Jaws; do we need it?

Answer:
Yes! The quality of the jaws depend from the character of the surfaces.
A whole lot of trials have been performed during the passed years (ie decades of years) in order to investigate different materials on the surfaces and patterns on the jaws (squares, waves, spirals etc). In short, the investigations shows that the original jaws with exactly this caracter of the blasted surface gives optimum performance concidering grip the gum and resulting in low standard deviations on the dissolution results. A bit depending on the formulation, already after a few runs (5-10 runs) the standard deviations may increase. Some gums are more sensible to wearing of the surfaces than other. Since cleaning from gum remains, always have to be performed we have decided that jaws should only be used once before cleaning, reblasting and qualification. In this way the jaws are always put aside after a run and are replaced by fresh and qualified jaws before next run. The operator may leave the cleaning etc to others (ie normally the Supplier).
The cleaning, blasting and qualification procedures are described in detail in the Manual. It is possible by the customer to perform the cleaning and blasting, but it must be made in a room separated from the analytical laboratory.