to be investigated, e.g. clinical samples, environmental samples, material for forensic medicine, etc.. The automatization of these processes has lead to a reduction of costs due to lab personnel, and played a role in avoiding human errors leading to contamination of the devices and reagents, wrong pipetting steps and consequently incorrect results,etc.

There is, however, a permanent need to improve these methods and devices in order to eliminate any potential risk of contamination and/or misleading results as well as to accelerate existing methods to safe resources and time.

## SUMMARY OF THE ~~INVENTION~~DISCLOSURE

There is a need to provide for an improved PCR sample preparation, e.g., the extraction of nucleic acids from a sample to be investigated, and/or for an improved PCR set-up.

The object of the present ~~invention~~ disclosure is solved by the subject-matter of the independent claims. Further embodiments and advantages of the ~~invention~~ disclosure are incorporated in the dependent claims.

The described embodiments similarly pertain to the system for PCR sample preparation and PCR set-up, the method of preparing a PCR, and the use of a tube holding device. Synergetic effects may arise from different combinations of the embodiments although they might not be described in detail hereinafter.

Furthermore, it shall be noted that all embodiments of the present ~~invention~~ disclosure concerning a method might be carried out with the order of the steps as described. Nevertheless, this has not to be the only and essential order of the steps of the method of the present ~~invention~~ disclosure. The skilled person gathers all kinds of different

orders and combinations of the method steps described herein, unless explicitly mentioned to the contrary hereinafter.

According to an exemplary embodiment of the ~~invention~~ disclosure, a system for PCR sample preparation and for PCR set-up is presented. The system comprises a loading device for receiving tubes. Hereinbelow tubes are generally referred to as "sample tubes", designating any type of vessel that is suited for taking up liquids and/or solids used in preparing or setting up PCR. The loading device comprises a first receiving section, and the first receiving section comprises at least a first receiving opening and a second receiving opening. Furthermore, the first receiving opening and the second receiving opening are adapted to respectively receive a sample tube. The system further comprises a tube holding device for being attached to the loading device.

In other words, the loading device and the tube holding device are configured in combination such that an attachment, a fixation, and/or a mounting of the tube holding device at or to the loading device is facilitated. The attachment between the loading device and the tube holding device is provided such that a fully automated PCR set-up and PCR sample preparation for the subsequent PCR is facilitated by the presented system. For the purpose of the attachment, fastening means or attachment means like protrusions, threads, or cooperative engaging means may be provided at the loading device and/or the tube holding device such that the desired attachment is achieved. This will be described in more detail hereinafter.

The provision of the tube holding device allows the user to cover unused tube positions, i.e. the unused receiving openings, of the loading device. The loading device may be embodied for example as a thermorack, e.g., a thermorack rotor disk, which may be used during the fully automated PCR set-up. Furthermore, the combination of the tube holding device and the loading device provides for the possibility of indicating assay specific reagent types by indicators or coding elements, like e.g. color labels or color indications, which according to the present

~~invention~~ disclosure, can be provided at the tube holding device. The use of specific coding elements on the tube holding device increases the practicability for the user and further increases the reliability of the PCR process. In particular, a failsafe mechanism is presented, such that the user places the sample tubes at the correct position. In other words, the presented system assists the user or a device in placing the sample tube at the correct position in the loading device. Additionally, the provision of the tube holding device in combination with the loading device facilitates a simultaneous placement and/or simultaneous removal of all tubes that are to be positioned at the loading device. This may accelerate the PCR sample preparation and PCR set-up process to a large extent.

The previously described advantages of the aspect of covering parts of the loading device of the present ~~invention~~ disclosure, the aspect of indicating by means of coding elements of the present ~~invention~~ disclosure, and the aspect of enabling for simultaneous placement and removal of a plurality sample tubes may especially provide for advantages during PCR sample preparation and PCR set-up when the loading device is embodied as a thermorack rotor and a correspondingly adapted tube holding device. The tube holding device may have an assay specific amount of receiving openings, which are positioned assay specific and which may comprise an assay specific coding elements for the sample tubes which are to be inserted into the arrangement.

The tube holding device may thus provide for a double functionality, as will be described hereinafter. First, the tube holding device may be configured to removeably attach the sample tube or tubes which are used for PCR sample preparation and for PCR set-up, such that the inserted sample tubes can be positioned and moved by means of moving the tube holding device. Second, the tube holding device may provide for a cover functionality, as the areas of the tube holder device between the receiving openings may be advantageously used to cover and/or close receiving openings of the loading device which in particular cases may not be used.

It should be noted that in this and every other exemplary embodiment, the tube holding device may comprise a plurality of receiving openings, and the loading device may also comprise a plurality of receiving openings larger than two. This provides for a system with increased possibilities of choosing between various numbers of different assays that can be performed in combination with assay specific tube holder devices. This leads to different possibilities of advantageous pipetting paths for the automated system or the user. Due to the large number of the receiving openings of the loading device and of the tube holding device, optimized selections of uncovered receiving openings is facilitated such that optimized pipetting paths from sample tubes in the receiving openings to PCR reaction chambers are facilitated. This will be explained in more detail with respect to the following Figs. 1 to 7, in which specific pipetting paths are described, such that the user gathers from the advantageous selection of receiving openings by combining the loading device with the assay specific tube holding device.

The presented system may provide for the advantage of pipetting directly into the second receiving section of the loading device, where PCR reaction chambers can be provided. In case the loading device is embodied as a thermorack rotor, pipetting directly into the rotor is facilitated by the present ~~invention~~ disclosure. This may be gathered from e.g. Fig. 1. Furthermore, simultaneous extraction set-up of e.g. four different assays may be facilitated by the presented system. In addition, simultaneous extraction of RNA and DNA in the same run is facilitated by the combination of the loading device and the tube holding device according to the present ~~invention~~ disclosure.

According to another exemplary embodiment of the ~~invention~~ disclosure, the system comprises one loading device and a plurality of different, assay specific tube holder devices.

A reservoir of different tube holder devices may be comprised by the presented system.

According to another exemplary embodiment of the ~~invention~~ disclosure, the tube holding device is a tube holding plate.

If desired, the tube holding plate may be embodied with an essentially circular shape. However, other shapes like rectangular or quadratic shapes may be possible embodiments of the tube holding plate. Furthermore, the tube holding device may be formed out of a metal or an alloy, but also polymer materials or other materials which are suitable for producing such a tube holding device may be used.

According to another exemplary embodiment of the ~~invention~~ disclosure, the tube holding device comprises at least a first receiving opening. Further, the tube holding device is attachable to the loading device such that the receiving opening of the tube holding device is aligned with at least one of the first receiving opening and the second receiving opening of the loading device and simultaneously covers the other of the first and the second receiving openings of the loading device.

Thus, in the attached configuration at least one receiving opening is covered and one is uncovered. In other words, this embodiment facilitates to cover, overcast and/or blanket the receiving openings of the loading device which are not used according to the intended assay and/or according to corresponding pipetting path performed by an automated pipetting device, which aspect of the present ~~invention~~ disclosure will be described in more detail. The loading device and the assay specific tube holding device can be arranged together such that the tube holding device covers and/or blankets the unused receiving opening of the loading device. The combination further facilitates that alignment of the receiving opening of the tube holding device is achieved with one of the receiving openings of the loading device. Due to this alignment, a sample tube according to a specific assay can be placed or inserted via the two aligned receiving openings, and can thereby be placed into the loading device for the subsequent PCR sample preparation and PCR set-up. In other words, by attaching the tube holding device to the loading device, a selection of the plurality of receiving

openings of the loading device is performed. Only those receiving openings of the loading devices are not covered by the tube holding device which receiving openings are to be used according to the presently used or desired assay.

This selection provides for an improved usability for the lab personnel and further provides for a simplification for the PCR sample preparation and for the PCR set-up.

According to another exemplary embodiment of the ~~invention~~ disclosure, the system comprises at least one a sample tube, wherein the sample tube is removeably attached to the receiving opening of the tube holding device.

In other words, the system provides for a tube holding device which is configured such that one or more sample tubes are moveable and receivable by the loading device and the tube holding device by aligning the opening of the tube holding device with one of the first and the second receiving openings of the loading device. Consequently, the sample tube, which is received, is held by the tube holding device is attached thereto such that the tube is moveable by moving the tube holding device. By attaching the tube holding device to the loading device, the held sample tube is inserted into the loading device. For the purpose of attaching the sample tube to the tube holding device, fixation or fastening means may be provided at the tube holding device and/or the sample tube. For example, purely mechanical means and forces may be used by means of an engagement of the collar of the sample tube with the circumferential surface of a receiving opening of the tube holding device. A corresponding provision or adaptation of the entangled diameters of the receiving openings and of the sample tube may be seen as another aspect of the present ~~invention~~ disclosure. For example, the sample tube may be received by the tube holding device in a hanging position in the receiving opening, as can be gathered from Fig. 8, for example. However, also other fastening and attaching means may be provided by the present ~~invention~~ disclosure, like for example magnetic forces, in order to attach the sample tube to the tube holding device. As a further embodiment, corresponding protrusions

or threads may be used in order to engage the sample tube and the tube holding device for the desired removable attachment, which can be released again, if desired.

According to another exemplary embodiment of the ~~invention~~ disclosure, the first receiving section of the loading device comprises a first plurality of receiving openings for receiving a sample tube, and the tube holding device comprises a second plurality of receiving openings for receiving a sample tube. Furthermore, in the attached position of the tube holding device at the loading device a part of the receiving openings of the loading device are aligned with corresponding receiving openings of the tube holding device and a remaining part of the receiving openings of the loading device are covered by the tube holding device.

This embodiment can easily be gathered from, for example, Figs. 1, 8, and the sequence of Figs. 13 to 15, where one loading device with three different tube holding plates for three different assays are shown.

According to another exemplary embodiment of the ~~invention~~ disclosure, a first plurality of sample tubes positioned for a first PCR assay is comprised, and a second plurality of sample tubes positioned for a second PCR assay is comprised by the system.
Furthermore, the tube holding device comprises one receiving opening for each sample tube such that all sample tubes are removeably attached to the tube holding device by means of the respective receiving opening for the tube holding device.

In other words, the tube holding device provides for two more or less separated sections or segments by means of which the sample tubes of the first assay or for the first assay are separated from the sample tubes for the second assay. In principle, this may be scaled up to each plurality of PCR assays, like for example a third plurality of sample tubes for a third PCR assay, a fourth plurality of sample tubes for a fourth PCR assay, a fifth plurality of sample tubes for a fifth PCR assay, and so on. The scope of this embodiment shall not be limited to the recitation of the fifth PCR assay,

but may be extended up to larger numbers if desired by the user. Therefore, by means of the combination of the loading device and the design of the tube holding device, all needed and different sample tubes for a plurality of PCR assays can simultaneously be inserted in the loading device and/or can simultaneously be removed, i.e. at once, from the loading device. This may accelerate the procedure of PCR sample preparation and PCR set-up.

According to another exemplary embodiment of the ~~invention~~ disclosure, a diameter of the receiving openings of the tube holding device is larger than a diameter of the sample tube, and wherein the diameter of the receiving openings of the tube holding device is smaller than a diameter of a collar of the sample tube.

This embodiment facilitates by means of gravitational forces only, that the tubes are hanging in the tube holding device due to an engagement between the rims of the receiving openings and the collars of the tubes. Therein, the rims may be provided by the circumferential surface of the openings of the tube holding device. If desired, additional rim elements may be provided such that a strengthened engagement between the tubes and the tube holding device is realized. Further aspects about the diameter combination of the receiving openings and the sample tubes used according to the present ~~invention~~ disclosure for PCR sample preparation and PCR set-up will be described with respect to Fig. 2 hereinafter.

According to another exemplary embodiment of the ~~invention~~ disclosure, the tube holding device comprises a coding element for coding information regarding an intended PCR-related purpose of the receiving opening

A coding element may be seen as an element of the system which is configured to provide for information, like e.g. mechanical, optical, electronical or magnetical information to a user or a device about the respective receiving opening of the assay specific tube holder device. This information may be detected by a mechanical,

optical, electronical or magnetical read out device, like e.g. a colour code scanner, of the presented system. In addition, abbreviations can be comprised as coding element at a receiving opening of the tube holder device. A coding element may for example be a mechanical pattern like differently shaped lines at or around a receiving opening. This may be gathered from Figs. 1 or 2 for example. A coding element may also be a chip which can be read out electronically or may be a colour code, like a colored surface. Further, text or abbreviations may be used to indicate to the user, which sample has to be positioned at the respective receiving opening.

The system may provide for sensing technologies which allows for recognizing the coding element and/or allows for reading out the information. By performing for example a color comparison between a color code on the tube holding device and a color code on a plurality of sample tubes, the correct sample tube may be selected based on the color comparison. Subsequently, the selected sample tube may be inserted into the corresponding receiving opening having the same color as the coding element.

According to another exemplary embodiment of the ~~invention~~ disclosure, the tube holding device comprises a coding element at each receiving opening for indicating which substance is to be positioned in the respective receiving opening by means of the sample tube.

According to another exemplary embodiment of the ~~invention~~ disclosure the coding element is a color code.

The color codes may also be seen as labels on the tube holding device to indicate the reagent type of each position, i. e. of each receiving opening, of the tube holding device. This embodiment of the tube holding device may prevent misplacing the tubes to wrong locations. For example, the color code may be provided as a color coded ring around a receiving opening. The PCR-related purpose indicated by means

of the coding element may for example be "water", "positive control", "primer and probe mixture (PPM)", "extraction control primer and probe mixture (ECPPM)" , "quantitative standard (QS)". However, also other indications may be used without departing from the scope of the present ~~invention~~ disclosure. In addition to colour codes, abbreviations can be comprised at each receiving opening of the tube holder device.

According to another exemplary embodiment of the ~~invention~~ disclosure, a color code is a colored surface of the tube holding device, and wherein the colored surface is close to or at the respective receiving opening. This embodiment may be gathered for example from the following Figs. 1 and 9.

According to another exemplary embodiment of the ~~invention~~ disclosure, the loading device is a PCR thermorack.

The PCR thermorack may be inserted into a thermocycler after the PCR sample preparation and PCR set-up has been performed by means of the presented system. As can be gathered from Fig. 17, the PCR reaction chambers which have been prepared during the PCR set-up process can directly be inserted by means of the loading device into a foil sealing device. Also fast and direct insertion into a thermocycler, in particular a PCR thermocycler, or also into an autoclaving device is facilitated by the presented loading device.

According to another exemplary embodiment, the loading device and the tube holding device have both a circular shape.

Consequently, a circular arrangement of PCR reaction chambers may be placed around the loading device, such that pipetting from the central part of the circular-shaped loading device towards the circumferential region of the loading device and into the PCR reaction chambers positioned there is facilitated.

According to another exemplary embodiment of the ~~invention~~ disclosure, the loading device comprises a second receiving section for receiving a plurality of PCR reaction chambers.

Such reaction chambers for PCR reagents may be gathered from, for example, Figs. 1, 5, 8, and 13. Such PCR reaction chambers may also be comprised by the system according to the present ~~invention~~ disclosure. The PCR set-up may be performed such that the desired liquid combination is provided within the PCR reaction chambers by pipetting the necessary reagents from the sample tube into the PCR reaction chambers. The combination of the tube holding device and the loading device allows for optimized pipetting paths, which will be explained in more detail for example with respect to following Figs. 5 and 7. As a further embodiment, the second receiving section may be a circumferential section around the first receiving section of the loading device. This may be gathered from for example Fig. 1.

According to another exemplary embodiment of the ~~invention~~ disclosure, the tube holding device expands horizontally along a first plane, wherein the first plane has a circular shape and cover a circular area of the loading device with the exception of at least one receiving opening of the loading device which is aligned with one of the receiving openings of the tube holding device.

In principle, a plurality of aligned receiving openings and a plurality of covered receiving openings can be realized by the attachment of the tube holder device to the loading device according to the present ~~invention~~ disclosure. Starting from this, the person skilled in the art is clearly aware of how to geometrically configure the tube holding device in order to cover specific receiving openings of the loading device, whereas simultaneously other receiving openings are released, unblocked or uncovered for being able to receive a sample tube.

According to another exemplary embodiment of the ~~invention~~ disclosure, the tube holding device comprises a handle for being grasped by a user. The handle facilitates inserting and/or removing the tube holding device into and/or from the loading device.

In order to facilitate and/or accelerate a fully automated PCR sample preparation and PCR set-up, an automatic exchange of assay specific tube holding devices is provided by the present ~~invention~~ disclosure. A grasping unit may be configured to exchange several assay specific tube holding devices and engage and disengage them respectively with the used loading device. A reservoir of different tube holder devices may be comprised by the presented system.

According to another exemplary embodiment of the ~~invention~~ disclosure, the tube holding device comprises a first surface segment of a first PCR assay, and comprises a second surface of a second PCR assay. The first surface segment comprises a plurality of receiving openings, and the second surface segment comprises a plurality of receiving openings. Therein, the first receiving opening and the second receiving opening, as defined previously, shall be understood to be comprised by the first and the second surface segment of the present embodiment. In other words, the tube holding device provides for two separated regions, wherein each region provides for the sample tubes necessary for providing all the reagents for a specific assay.

According to another exemplary embodiment of the ~~invention~~ disclosure, the first surface segment comprises at least one color code indicating a first color of a receiving opening, and the second surface segment comprises at least one color code indicating a color code of a receiving opening, wherein the first and the second colors are the same. In general, the first and second segments may comprise a coding element, as described herein.

According to another exemplary embodiment of the ~~invention~~ disclosure, the first and the second PCR assay segments of the tube holding device are arranged relative to each other in a geometrical manner which is chosen from the group comprising: the first segment is a first segment of circle and the second segment is a second segment of circle, the first and second segments are divided on the circular tube holding device by a straight line or by a curved line passing a centre of the circular tube holding device, the receiving openings of the first and the second segments are symmetric to a central point of the tube holding device, and any combination thereof.

For example, the straight division between the two segments may be gathered from Fig. 1, whereas the curved division between the first and second segments can be gathered from for example Fig. 2 and Fig. 11. The point-symmetric distribution of the assay specific receiving opening distribution as shown for example in Fig. 5 may provide for the possibility of improved pipetting paths, which is described in more detail with respect to Fig. 5.

According to another exemplary embodiment of the ~~invention~~ disclosure, each receiving opening of the tube holding device is marked with a color code.

According to another exemplary embodiment of the ~~invention~~ disclosure, the tube holding device comprises at least one attachment means for releasable attaching the tube holder device to the loading device.

Attachment means, like for example the use of magnetic forces or threads may be seen as in the scope of this exemplary embodiment.

According to another exemplary embodiment of the ~~invention~~ disclosure the attachment means is configured to be inserted into a receiving opening of the loading device to stabilize the attachment of the tube holding device at the loading device.

In another more specified embodiment, the attachment means may be seen as stabilizing protrusion elements. Engaging protrusions with corresponding engagement recesses, like e.g. receiving openings, at the loading device may be presented according to this exemplary embodiment.

According to another exemplary embodiment of the ~~invention~~ disclosure, the system comprises a cover which is configured for simultaneously covering the loading device and the tube holding device.

According to an even more specified embodiment, a system with the cover is autoclaveable and is easy to be decontaminated. Consequently, this embodiment presents an autoclaveable system with a cover, a loading device, and a tube holding device. The cover may be optically transparent or optically not transparent. The cover may prevent the cross carry over during a PCR sample preparation process in the presented system.

According to another exemplary embodiment of the ~~invention~~ disclosure, the cover has essentially a circular shape and is adapted to the shape of the tube holding device and/or the shape of the loading device.

According to another exemplary embodiment of the invention, the system comprises a scanner, wherein the scanner is configured for scanning at least one element chosen from the group comprising elution plate, extraction reagents, assay reagents, sample tubes, and any combination thereof. The scanner is configured to transmit scanned data to a calculating unit.

The scanner may be embodied as for example a handheld scanner. In particular, the scanner may be configured to scan barcodes used for transporting information. Therefore sample information can be gathered by the scanner via for example barcode scanning and may be transmitted to a calculating unit. The calculating unit

may create data for a PCR thermocycler in a thermocycler readable data format. This may further accelerate the complete PCR procedure and may result in a high throughput system for the user.

According to another exemplary embodiment of the ~~invention~~ disclosure, the system may comprise the calculating unit which is configured to generate sample information in a thermocycler readable data format.

Thus, interfacing data between the system for PCR sample preparation and for PCR set-up one the one hand and the thermocycler on the other hand is also presented by the present ~~invention~~ disclosure.

According to another exemplary embodiment of the ~~invention~~ disclosure, the system comprises the thermocycler, wherein the thermocycler and the calculating unit are in communication with each other. The thermocycler is configured to automatically perform a PCR in a received PCR reaction chamber based on the sample information received in the thermocycler readable data format from the calculating unit.

Therein, wireless or wired communication between the thermocycler and the calculating unit may be used according to this embodiment of the present ~~invention~~ disclosure. A fully automated system providing PCR sample preparation, PCR set-up, and carrying out the complete PCR may thus be presented by the present ~~invention~~ disclosure.

According to another exemplary embodiment of the ~~invention~~, the tube holding device is configured assay specific with respect to a geometrical distribution of the receiving openings.

According to another exemplary embodiment, the system comprises a first tube holding device and a second tube holding device, wherein the tube holding devices are configured assay specific respectively, and wherein the respective configuration

of the first tube holding device is different from the second tube holding device with respect to the distribution of the receiving openings.

According to another exemplary embodiment of the ~~invention~~ disclosure, the first receiving section is centrally positioned at the loading device. Furthermore, the loading device is adapted to receive PCR reaction chambers at the second receiving section positioned exterior to or outside of the central position of the first receiving section. Furthermore, the tube holding device is configured for a specific assay with respect to the geometrical distribution of the receiving openings, such that straight pipetting paths from a receiving opening with a coding element for a sample tube containing a specific concentration of a target molecule into the second receiving section are facilitated. Furthermore, this embodiment facilitates that pipetting paths cross covered receiving openings of the loading device only.

As can be gathered from following Fig. 7, such a distribution of receiving openings of the tube holding device facilitates to use direct pipetting paths from the receiving openings towards a circumferential region of the tube holding device, whereby only covered sections of the below lying loading device are crossed. The pipetting paths are indicated in Fig. 7 by the dashed line arrows. This may further increase the security level of carrying out PCR sample preparation and PCR set-up with the presented system. Unused and covered receiving openings of the loading device are not contaminated during the pipetting procedure in case the pipetting paths are chosen as shown within Fig. 7.

According to another exemplary embodiment of the ~~invention~~ disclosure, the tube holding device comprises a plurality of receiving openings at which an intended receipt of a sample tube containing a specific concentration of a target molecule is indicated respectively. This may be true for at least a part of the plurality of receiving openings. The positions of the receiving openings is configured such that a path between a central region of the tube holding device and an edge region of the tube

holding device crosses receiving openings, at which an intended receipt of a sample tube with a specific concentration of a target molecule is indicated, from low concentration to high concentration.

In the context of the present ~~invention~~ disclosure the term "edge region" shall not be understood such that an edge is necessarily comprised. An "edge region" may also be understood as a peripheral region or a boundary region.

For this and every other embodiment of the present ~~invention~~ disclosure such an indication may be done by a coding element, an abbreviation or a color code as described herein. This exemplary embodiment will be described in more detail with respect to the embodiment of Fig. 5. This embodiment may also advantageously decrease the contamination risk of a surface segment of the system of the present ~~invention~~ disclosure during a PCR set-up process.

According to another exemplary embodiment of the ~~invention~~ disclosure, the tube holding device comprises a first receiving opening at which an intended receipt of a sample tube with a first concentration of a target molecule is indicated. The tube holding device comprises a second receiving opening at which an intended receipt of a sample tube with a second concentration of a target molecule is indicated. Furthermore, the first and the second receiving openings are positioned relative to each other, such that straight pipetting paths from a central region to an edged region of the tube holding device are facilitated, which paths pass the first and second receiving openings from low to high concentrations.

Consequently, in a further exemplary embodiment of the ~~invention~~ disclosure, a first tube holding device is removed from the loading device and is replaced by a second loading device in order to facilitate a further PCR set-up with different requirements. Consequently, in this and every other exemplary embodiment of the ~~invention~~ disclosure, the loading device can be combined with a plurality of different tube holding devices.

In one aspect, there is provided a system for PCR sample preparation and for PCR set-up, the system comprising a loading device for receiving sample tubes for setting up a

PCR, wherein the loading device comprises a first receiving section, wherein the first receiving section comprises at least a first receiving and a second receiving opening, wherein the first receiving opening and the second receiving opening are adapted to respectively receive a sample tube, the system further comprising a tube holding device for being attached to the loading device, wherein the tube holding device comprises at least a first receiving opening, and wherein the tube holding device is attachable to the loading device such that the receiving opening of the tube holding device is aligned with at least one of the first receiving opening and the second receiving opening of the loading device and simultaneously covers the other of the first and the second receiving openings of the loading device.

According to another exemplary embodiment of the ~~invention~~ disclosure, a method of preparing a PCR is presented. The method comprises the steps of providing for a loading device, providing for a tube holder device and attaching the tube holder device to the loading device. Furthermore, the loading device configured for receiving sample tubes for setting up a PCR and the loading device comprises a first receiving section. The first receiving section comprises at least a first and a second receiving opening wherein the first receiving opening and the second receiving opening are adapted to respectively receive a sample tube.

According to another exemplary embodiment of the ~~invention~~ disclosure, the tube holder device comprises at least a first receiving opening. The method of this embodiment further comprises the step of aligning the receiving opening of the tube holder device with one of the first receiving opening and the second receiving opening of the loading device and thereby simultaneously covering the other of the first and the second receiving openings. The presented method of the present ~~invention~~ disclosure facilitates covering unused receiving sections by means of attaching the tube holder device to the loading device. Further, the method may make use of indicating assay specific reagent types by for example colored labels or by other color indicators. Combining the tube holder device with the loading device enables for simultaneous placement of sample tubes and enables for simultaneous removal of sample tubes in particular of all used tubes from the loading device.

According to another exemplary embodiment of the ~~invention~~ disclosure, method further comprises the steps of removably attaching a sample tube to the tube holding device and inserting the sample tube into a receiving opening of the loading device by attaching the tube holding device to the loading device.

In other words, the spatial distribution of the receiving openings of the tube holder device is adapted to the spatial distribution of the receiving openings of the loading

device and is based on the requirements of the assay to which the tube holder plate is dedicated. The step of attaching may be done by a user or by an automated device.

According to another exemplary embodiment of the ~~invention~~ disclosure, the method further comprises the step of simultaneously separating the tube holder device and the sample tube received by the loading device from the loading device by grasping the tube holder device and removing the tube holder device from the loading device.

In other words, all sample tubes used within the loading device can be removed at once by grasping the tube holder device and moving it away from the loading device. Therefore, an improved placement automation is provided by the present ~~invention~~ disclosure.

According to another exemplary embodiment of the ~~invention~~ disclosure, the method comprises the step of simultaneously removing a first plurality of sample tubes for a first PCR assay and a second plurality of sample tubes for a second PCR assay from the loading device by grasping the tube holder device and removing the tube holder device from the loading device.

This embodiment emphasizes the high throughput abilities of the presented method, as a plurality of PCR assays may be prepared simultaneously and all needed sample tubes can be removed at once. This embodiment is not limited to a first and a second PCR assay but may be extended to a larger number of PCR assays.

According to another exemplary embodiment of the ~~invention~~ disclosure, the method comprises the step of inserting a stabilizing protrusion element of the tube holder device into a receiving opening of the loading device during attaching the tube holder device to the loading device.

In order to stabilize the attachment and/or fastening of the tube holder device at the loading device stabilizing protrusion elements may be used. As a general remark it

should be noted, that general attachment means may be provided which during attaching the tube holder device to the loading device create the attachment via for example a integral connection, form closure or via for example threads or corresponding engaging elements.

According to another exemplary embodiment of the ~~invention~~ disclosure, the method comprises the step of covering unused receiving openings of the loading device by the tube holding device.

It may be seen as an important aspect of the ~~invention~~ disclosure that simultaneously another receiving opening than the covered receiving opening of the loading device is uncovered, i. e. aligned with a receiving opening of the tube holding device.

According to another exemplary embodiment of the ~~invention~~ disclosure, the tube holding device comprises at least a first opening having a color code indicating a first color and a second opening having a color code indicating a second color. The method of the presented embodiment comprises the steps of providing a sample tube with a color code indicating a third color, selecting the receiving opening of the tube holding device which has the same color as the color code of the sample tube and inserting the sample tube into the selected receiving opening of the tube holding device.

In other words, based on a color comparison, the correct receiving opening of the loading device for the process of sample preparation is identified.

According to another exemplary embodiment of the ~~invention~~ disclosure, the method comprises the step of covering the loading device and the tube holding device and inserted sample tubes by placing a cover to the loading device, the tube holding device, and the inserted sample tubes.

If desired, autoclavability can be reached by this covering process. In other words, the presented system can be placed in an autoclave to perform decontamination. If desired the loading device and the tube holding device and the cover can be configured to withstand high pressure of saturated steam at approximately 121 °C for around 15 to 20 minutes, which is typical for an autoclave.

According to another exemplary embodiment of the ~~invention~~ disclosure, the method comprises the step of scanning data of at least one element, chosen from the group comprising elution plate, extraction reagents, assay reagents, sample tubes, and any combination thereof. The method also comprises the step of transmitting the scanned data to a calculating unit for PCR purposes.

The system of the present ~~invention~~ disclosure is able to recognize and set-up the desired PCR reaction on the loading device to which the tube holding device has been arranged. A wireless or wirebound communication may be provided between a scanner, for example a handheld scanner, and a calculating unit which may be comprised by the system, or which may also be comprised by a computer which is in communication with the system of the present ~~invention~~ disclosure. The calculating unit in any case may be provided in communication with a thermocycler and which unit may generate sample information in a thermocycler readable data format. These data in the thermocycler readable data format may be transmitted to the thermocycler to initiate the PCR. Furthermore, performing a PCR in a received PCR reaction chamber by the thermocycler based on the sample information received in the thermocycler readable data format may be seen as another exemplary embodiment of the ~~invention~~ disclosure. Further aspects related to this embodiment may be gathered from Figs. 19 and 20.

According to another exemplary embodiment of the ~~invention~~ disclosure, the method comprises the step of indicating at each receiving opening of the tube holding device which respective substance is to be positioned in the respective receiving opening.

This may be done by a coding element. This embodiment ensures that the assay specific configuration or adaption of a tube holding device is followed by the user. In particular, the user will recognize the indication provided at the tube holding device and can easily insert the corresponding sample tube into the receiving opening in a failsafe manner. In other words, a failsafe mechanism for the user is presented, by means of which the user is guided through the process of inserting all the necessary sample tubes into the loading device.

According to another exemplary embodiment of the ~~invention~~ disclosure, the first receiving section is centrally positioned at the loading device. This embodiment comprises the step of receiving PCR reaction chambers by the loading device at the second receiving section positioned exterior of the central position of the first receiving section. Furthermore, the presented method comprises the step of pipetting along a straight path from a receiving opening with an coding element for a sample tube containing a specific concentration of a target molecule into the second receiving section, which path crosses covered receiving openings of the loading device only.

This advantageous embodiment of the present ~~invention~~ disclosure may be gathered from following Fig. 7. The configuration of the receiving openings of the tube holding device is provided in such a way that the desired pipetting along the straight path towards the received PCR reaction chambers in the circumferential second section is facilitated.

According to another exemplary embodiment of the ~~invention~~ disclosure, the method comprises the steps of indicating at a plurality of the receiving openings of the tube holding device an intended receipt of a sample tube containing a specific concentration of a target molecule, respectively. Furthermore, the step of pipetting along a path between a central region of the tube holding device and an edged region of the tube holding device and thereby crossing receiving openings at which an intended receipt of a

sample tube with a specific concentration of the target molecule is indicated is performed from low concentration to high concentration.

In other words, this method ensures that pipetting paths are chosen in combination with the underlying tube holding device with its assay specific opening distribution such that crossing a sample tube with a lower concentration of the target molecule compared to the concentration where the pipetting process started is avoided.

According to another exemplary embodiment of the ~~invention~~ disclosure, the method comprises the steps of indicating at a first receiving opening of the tube holding device an intended receipt of a sample tube with a first concentration of a target molecule, indicating at a second receiving opening of the tube holding device an intended receipt of a sample tube with a second concentration of a target molecule, and providing the first and the second receiving openings at the tube holding device at positions relative to each other, such that straight pipetting paths from a central region to an edged region of the tube holding device are facilitated from low to high target molecule concentrations.

In one embodiment, there is provided a method of setting up a PCR, the method comprising the steps of providing for a loading device, which loading device is for receiving sample tubes for setting up a PCR, providing for a tube holding device, wherein the loading device comprises a first receiving section, wherein the first receiving section comprises at least a first and a second receiving opening, wherein the first receiving opening and the second receiving opening are adapted to respectively receive a sample tube; wherein the tube holding device comprises at least a first receiving opening, the method further comprising the step of attaching the tube holding device to the loading device ; aligning the receiving opening of the tube holding device with one of the first receiving opening and the second receiving opening of the loading device and simultaneously covering the other of the first and the second receiving openings .

According to another exemplary embodiment of the ~~invention~~ disclosure, the use of the tube holding device as defined in one of the previously defined embodiments for PCR setup is presented.

In one embodiment, there is provided the use of a tube holding device as disclosed herein for PCR set-up.

These and other features of the ~~invention~~ disclosure will become apparent from and elucidated with reference to the embodiments described hereinafter.

According to another exemplary embodiment of the ~~invention~~ disclosure, a computer program element for PCR sample preparation and for PCR set-up which, when being executed by a processor, is adapted to carry out the steps as described herein and in the claims.

The computer program element presented herein may be part of a computer program, but it can also be an entire program by itself. For example the computer program

element may be used to update an already existing computer program to get to the present ~~invention~~ disclosure. The computer readable medium may be seen as a storage medium, such as for example, a USB stick, a CD, a DVD, a data storage device, a hard disk, or any other medium on which a program element as described above can be stored.

## BRIEF DESCRIPTION OF THE DRAWINGS

Exemplary embodiments of the invention will be described in the following drawings.

Figs. 1 and 2 schematically show different systems for PCR sample preparation and for PCR set-up according to exemplary embodiments of the invention.

Fig. 3 schematically shows a loading device which can be used for a PCR sample preparation and for PCR set-up according to another exemplary embodiment of the invention.

Figs. 4 to 7 schematically show different systems for PCR sample preparation and for PCR set-up according to exemplary embodiments of the invention.

Fig. 8 schematically shows a system with a cover according to another exemplary embodiment of the invention.

Fig. 9 schematically shows a tube holding device which can be used for PCR set-and PCR sample preparation according to another exemplary embodiment of the invention.

Figs. 10 to 16 schematically show different systems for PCR sample preparation and for PCR set-up according to exemplary embodiments of the invention.