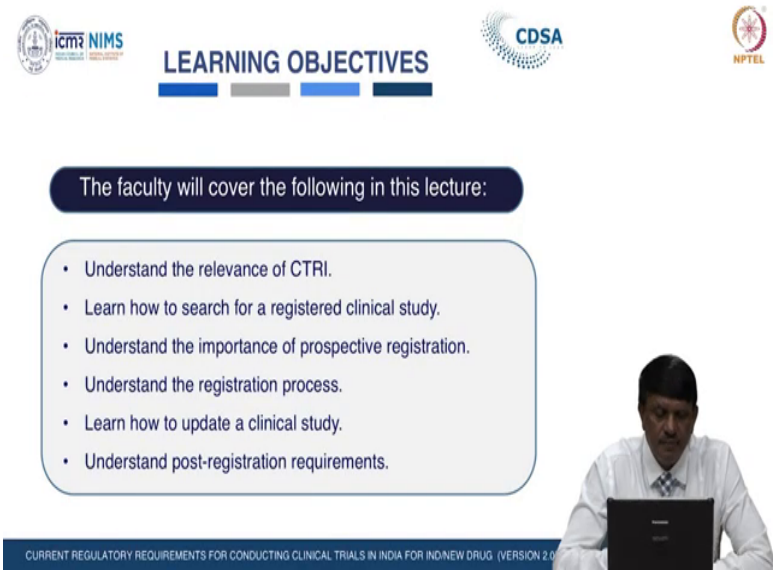
Current Regulatory Requirements for Conducting Clinical Trials in India for IND/New Drug Version 2.0

Dr. Vishnu Vardhan Rao
Department of Biotechnology
Indian Institute of Technology, Madras

Lecture – 27B
ONLINE SUBMISSION (CTRI)

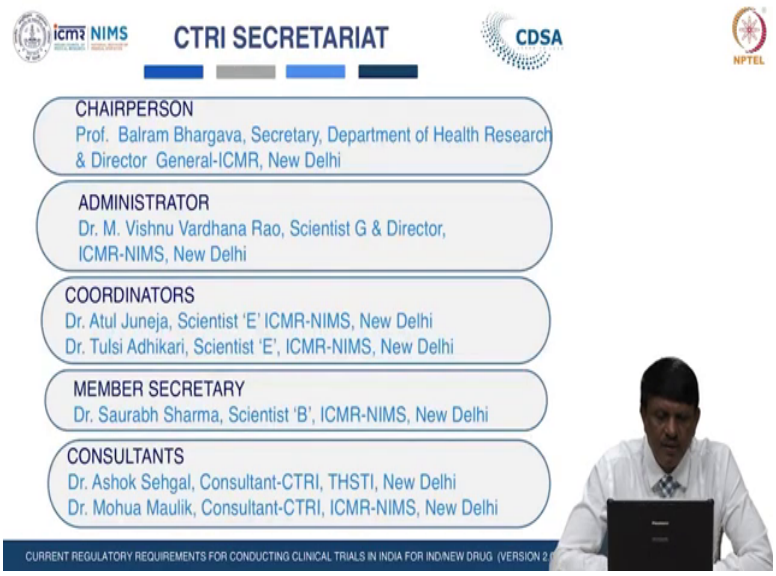
Welcome, all I am Dr. Vishnu Vardhana Rao director ICMR National Institute of Medical Statistics and Administrator to Clinical Trial Registry India. Today we are going to discuss about current regulatory requirements for conducting clinical trials in India. The this lecture is lecture number 23 myself and my colleagues are going to discuss about Online Submission of clinical trial registry India.

(Refer Slide Time: 00:39)



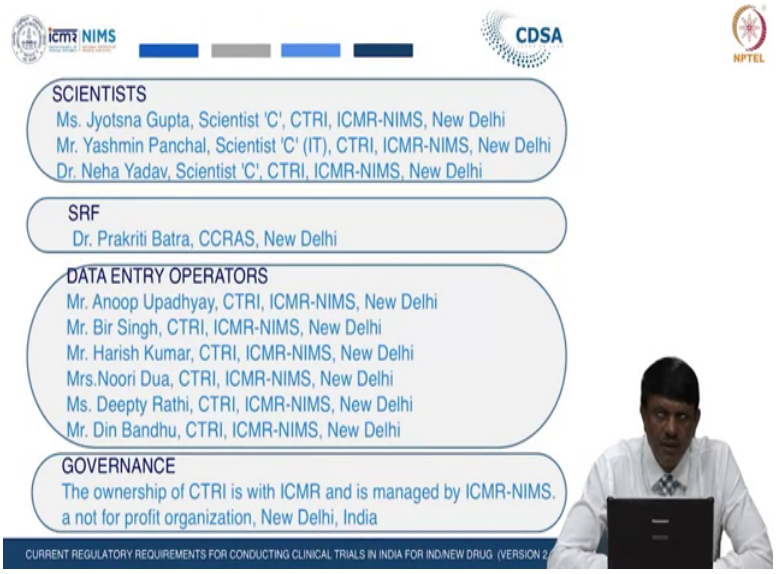
So, the objectives of this (Refer time: 00:40) lecture being understand the relevance of the CTRI, learn how to search for registered clinical studies, understand the importance of prospective registration, understand the registration process, learn how to update a clinical study, understand post registration requirements. These are all the things which we are going to we are going to talk and we are going to learn about this.

(Refer Slide Time: 01:08)



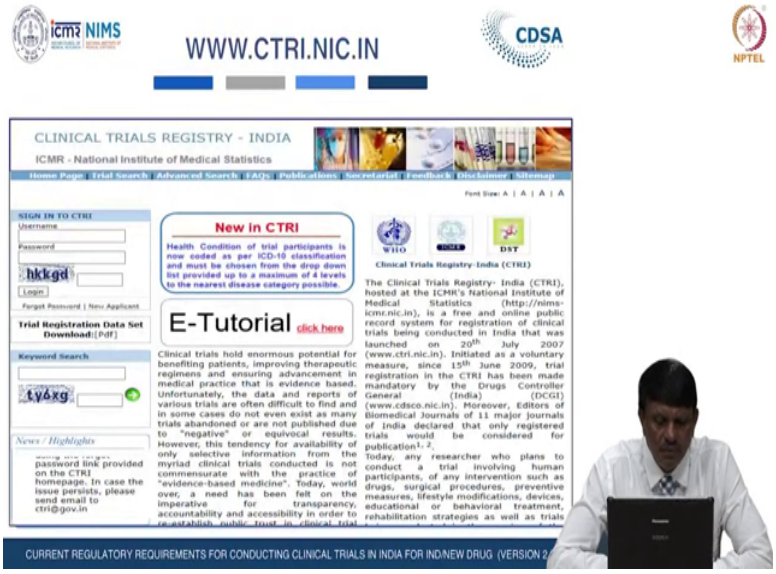
So, CTRI has the secretariat of I mean NIMS and New Delhi ICMR, NIMS New Delhi. And the chain person being Professor Balram Bhargava secretary D HR and DG ICMR administrator being myself I am M Vishnu Vardhana Rao. I am Director of National Institute of Medical Statistics ICMR as well as administrative CTRI and have we have two coordinators and one member secretary and we have two consultants.

(Refer Slide Time: 01:39)



There are three scientists which life science background where they screen the trials and has been followed by six data entry operators who does the registration. And we have one computer scientist where he looks after all the software and hardware requirements of the registry.

(Refer Slide Time: 02:01)

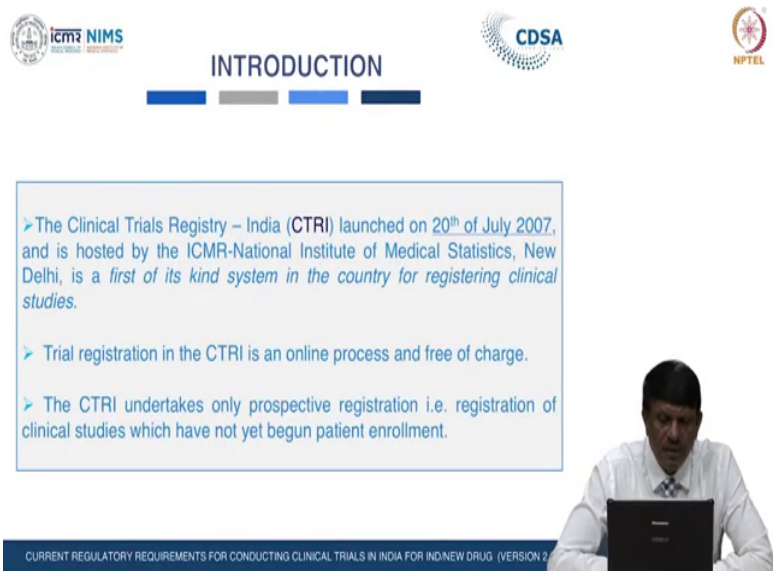


And this is the structure of the CTRI where you can see on the screen. And this is the website of the CTRI this is the homepage for that and you can see all the ingredients of the home site here homepage here. And the once you start opening the CTRI this is the homepage you will see and we can start entering your register trials.

(Refer Slide Time: 02:27)

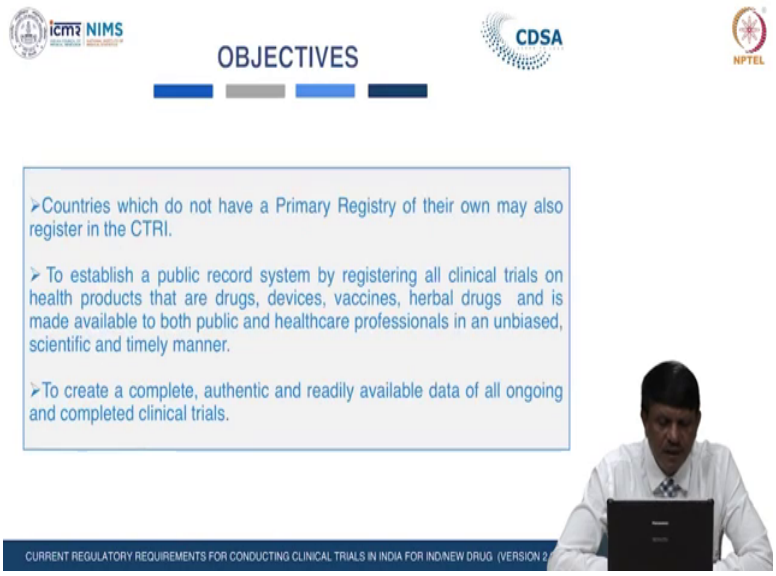
The importance of the clinical trial registration is the registration of all interventional trials is a scientific, ethical and moral responsibility which is stated by WHO. Every clinical trial must be registered in a publicly accessible database before recruitment of the first subject that is the declaration of Helsinki 2008. When in doubt register WHO; that is the World Health Organization statement.

(Refer Slide Time: 02:57)



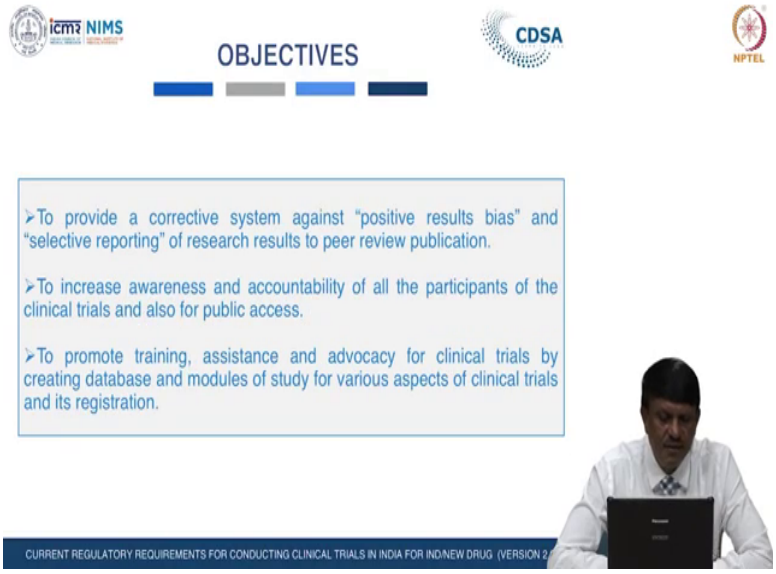
About this CTRI the Clinical Trial Registry India CTRI launched in on 20th of July 2007, and hosted by the ICMR National Institute Medical Statistics New Delhi. It is a first of its kind system in the country for registering clinical studies, trial registration in the CTRI is an online process and free of charges. The CTRI undertakes only prospective registrations that is registration of the clinical trial studies which have not yet begun patient enrollment.

(Refer Slide Time: 03:35)



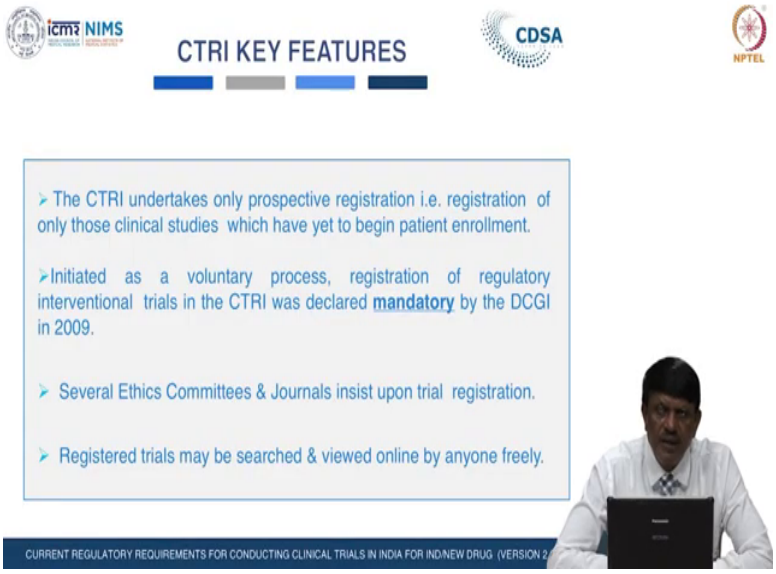
Countries which do not have the Primary Registries of their own also can register in the clinical trial registry India. The objectives of the CTRI are as follows; the first objective being the establish a public record system by registering all clinical trials on health products that are drugs, devices, vaccines, herbal drugs and is made available to both public and healthcare professionals in an unbiased scientific and timely manner. To create a complete, authentic and readily available data of all ongoing uncompleted clinical trials.

(Refer Slide Time: 04:17)



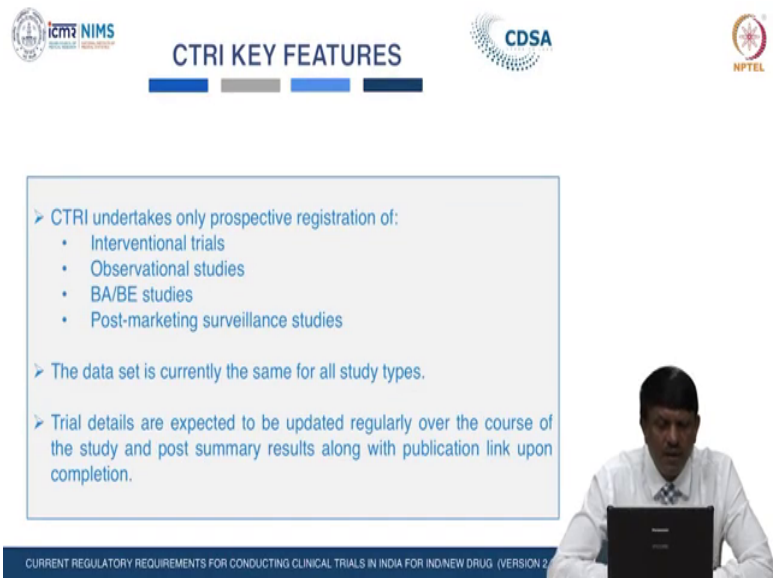
To provide a corrective system against positive results bias and selective reporting of research results to peer reviewed publications. To increase awareness and accountability of all patient participants of the clinical trials and also for public access, the process of training assistant and advocacy for clinical trials by creating database and modules of the study for various experts of clinical trials and its registration.

(Refer Slide Time: 04:48)



The key features of the CTRI are the CTRI undertakes only prospective registration that is registration of the only those clinical studies which have yet to begin of the patient enrollment. Initiated as a voluntary process registration of interventional trials in the CTRI was declared mandatory by the DCGI in 2009, several ethical committees and journals insist upon trial registration. Registered trials may be searched and reviewed online by any of the any of the any person freely.

(Refer Slide Time: 05:29)

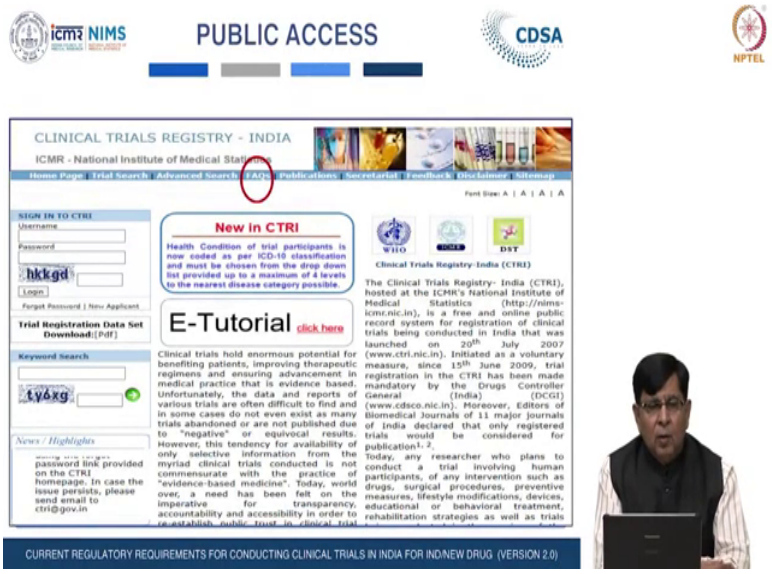


The key features of the CTRI, CTRI undertakes only prospective registration that is interventions trials, observational trials, bioavailability and bioequivalent studies, post marketing, marketing surveillance studies. The data set is currently the same for all study types trial details are expected to be updated regularly over the course of study and post summary results along with the publication link upon completion of the trial.

(Refer Slide Time: 06:05)

So, the there are three levels of access in this these are these will be taken up by my colleagues in subsequent lectures. And I also want to convey to you for the purpose of the convenience during this presentation, clinical trial and clinical studies are will be used interchangeably.

(Refer Slide Time: 06:33)



So, this we have to note down these two words we have been using that interchangeably. Welcome, back friends you just now heard Dr. Vishnu Vardhana Rao Administrator Clinical Trial Register India, who gave the overall background of the clinical trial registration and the objectives of the registration process. As you know that this is housed at National Institute of Medical Statistics ICMRs Institute at New Delhi, I will take you further on the levels of access.

I am Dr. Atul Juneja Coordinator at Clinical Trial Registry India. Let me tell you that the clinical trial registry has three levels of access; one is public followed by the registrant and administrator. The public access is important it does not require any registration or user id, any prospect resistant can have a look at this before going for any registration process.

It is possible to search and view already registered trials download the registration data set and the publications by CTRI can also be viewed on this access, one can also go to e module where the various process of registration is being explained. There is another section called frequently asked questions, it forms an important part of any system, so it is CTRI. Prospective registrant is advised to have a look at this section before proceeding for trial registration.

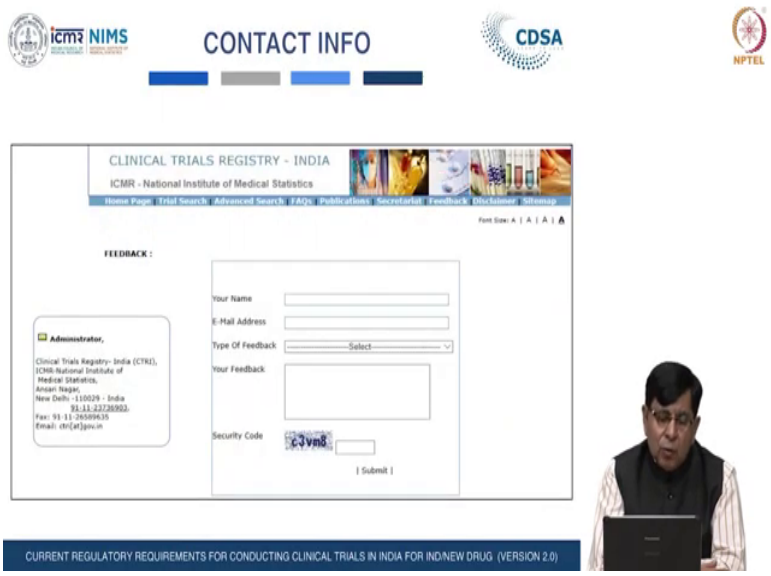
(Refer Slide Time: 07:57)

(Refer Slide Time: 08:00)

The trial registration data set can be downloaded which can be used for referencing and viewing, just remember it is used for referencing and viewing the registration process has to be done only online, I emphasize that it has to be done only online.

(Refer Slide Time: 08:13)

(Refer Slide Time: 08:20)



The contact section, in this section one can float any query to CTRI administrator and CTRI would be more than happy to answer you at the earliest.

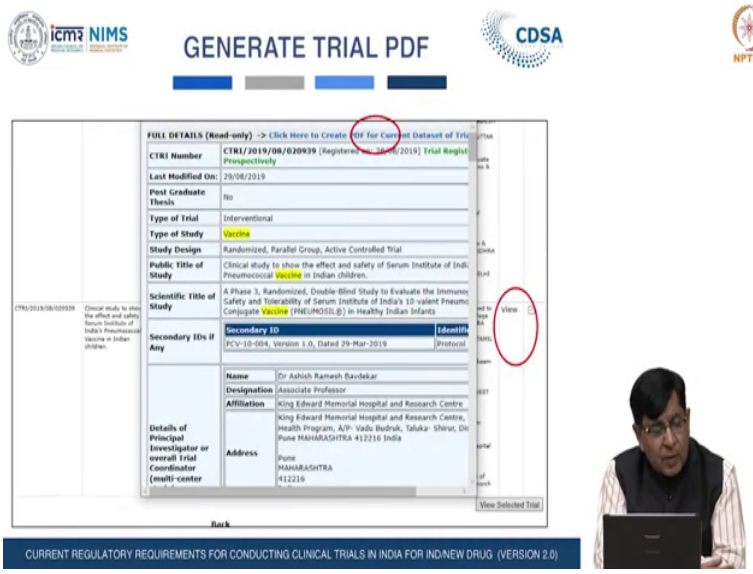
(Refer Slide Time: 08:23)

Then is a search option, the search options are basic search and the advanced search, in the advanced search where trials can be searched more precisely.

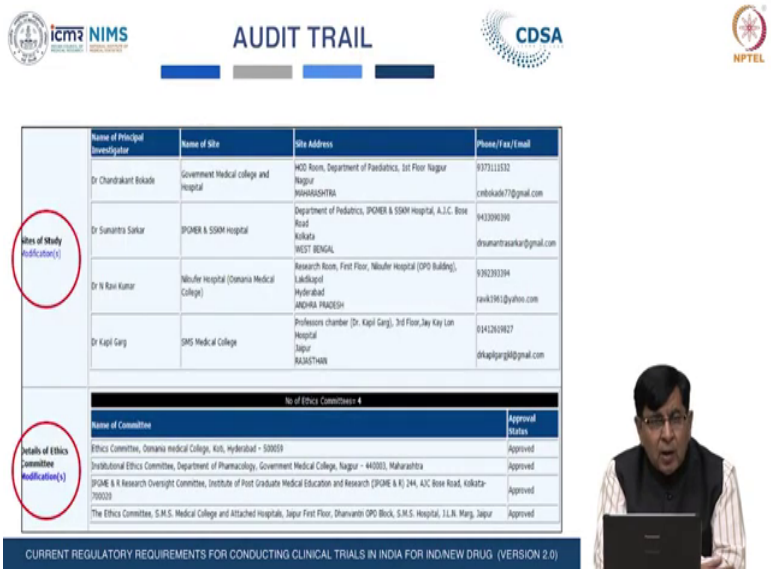
(Refer Slide Time: 08:30)

This would provide all information on registered trials including in the PDF format. Then there is also possible to view the sequence of modifications done by the triallist to various data items such as change in sample size etcetera which is known as audit trail.

(Refer Slide Time: 08:43)

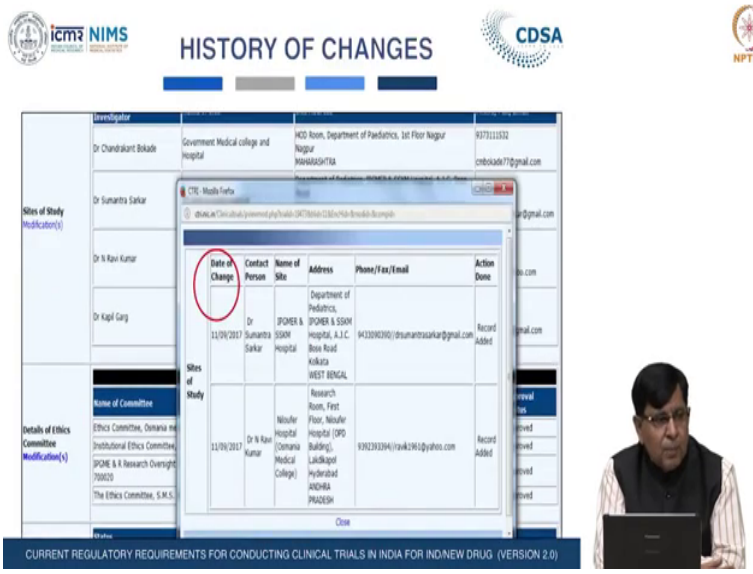


(Refer Slide Time: 08:45)



This is one of the important features of Clinical Trial Registry India.

(Refer Slide Time: 08:48)



(Refer Slide Time: 08:50)

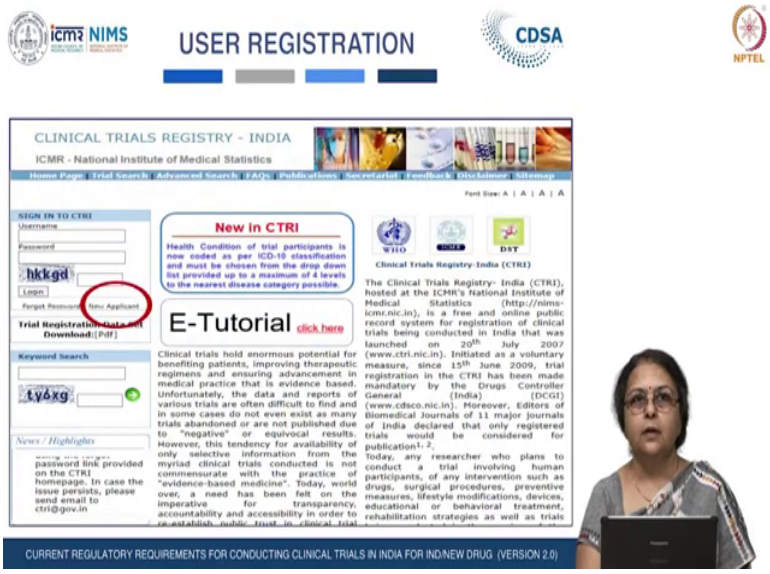
(Refer Slide Time: 08:52)

Then coming on to e module further by clicking on e module section, the registrant is taken to presentation with audio, which describes the detail process of trial registration this video audio video is about for 2 hours thank you so much. And to take you further on the registrant access I will request my colleague to explain further thank you.

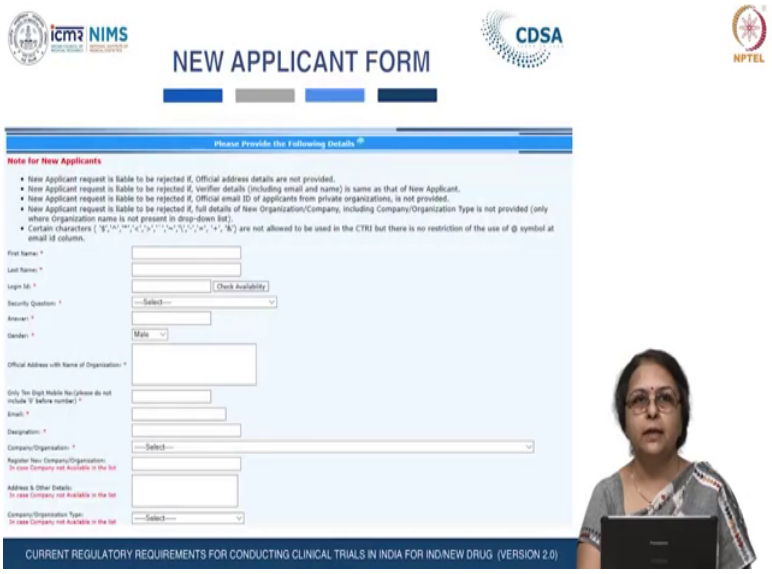
(Refer Slide Time: 09:13)

Welcome, Dr. Atul Juneja just described the public access to the CTRI, I am Dr. Mohua Maulik consultant with the CTRI and I will be discussing the second level of access to the CTRI that is of the registrant. A registrant is one who is authorized to register clinical trials, although anyone may be a registrant the it is the responsibility of the principal investigator and the primary sponsor to ensure that a clinical trial is registered in the CTRI. Registration in the CTRI is needed to gain access to this facility, the on the homepage of the CTRI you may register as a new applicant by clicking the new applicant button.

(Refer Slide Time: 09:53)

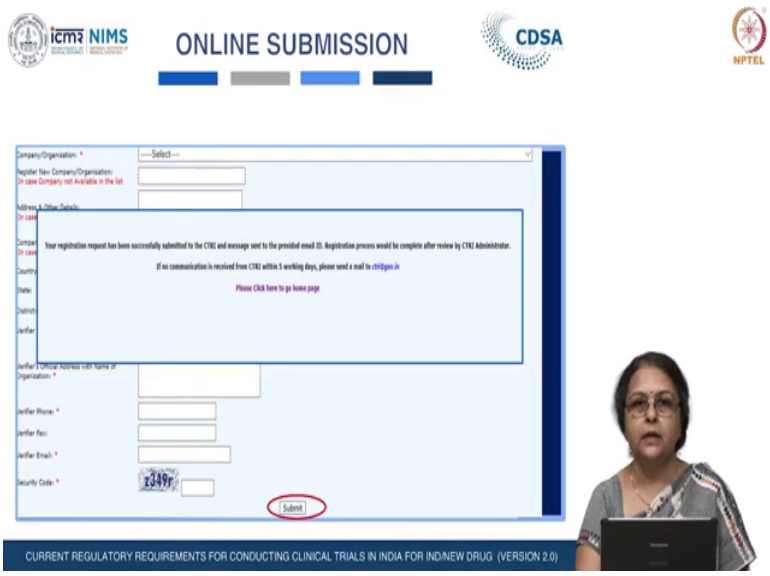


(Refer Slide Time: 09:58)



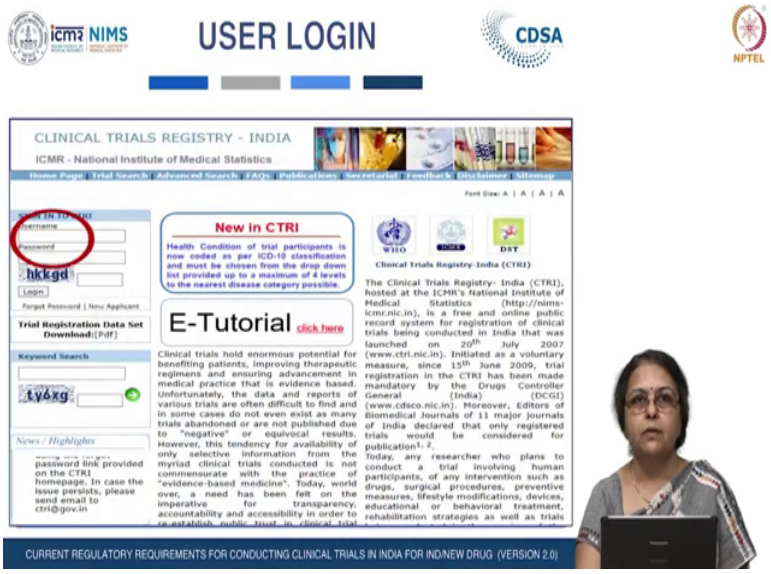
This will take you to the new applicant form, instructions to fill the new applicant form and likely issues to be faced are listed right on top, take a few moments to read these before proceeding to fill the form online.

(Refer Slide Time: 10:20)



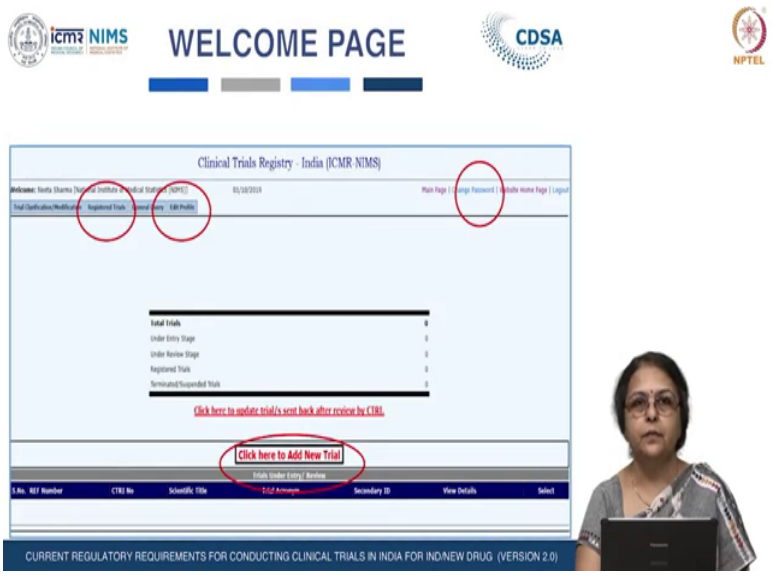
Once all the details have been filled click on the submit button, if the form is submitted successfully login credentials such as the username and password will be mailed to the provided email id, subsequently a second confirmatory mail will activate these username and password. In case, of failure to receive email from the CTRI please check junk or spam mail before contacting CTRI, in case an incorrect email id is provided there will be failure to receive these emails.

(Refer Slide Time: 11:57)



Once your credentials are activated you may login to your account in the CTRI.

(Refer Slide Time: 11:04)

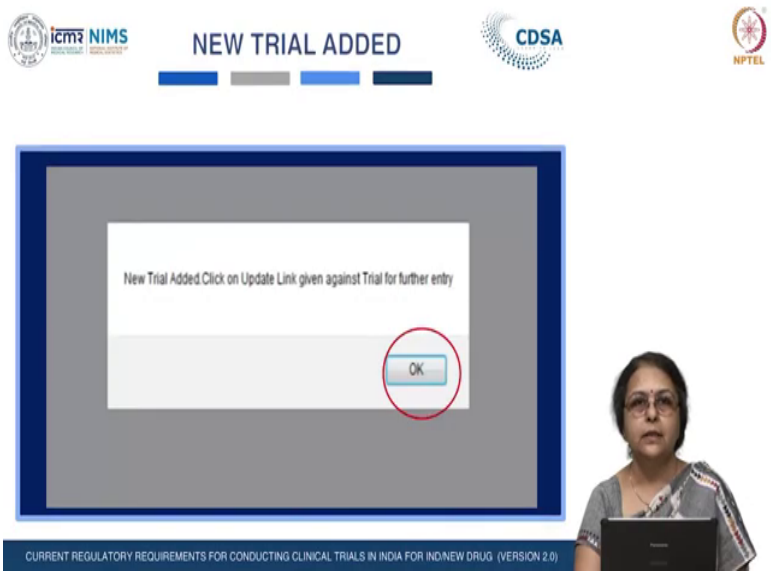


This is your personal welcome page on the CTRI, where several facilities and options are available such as viewing registered trials, editing your profile all at all profile features may be edited such as email id, name etcetera, password may also be changed. To upload your new clinical trial data click on the add new button.

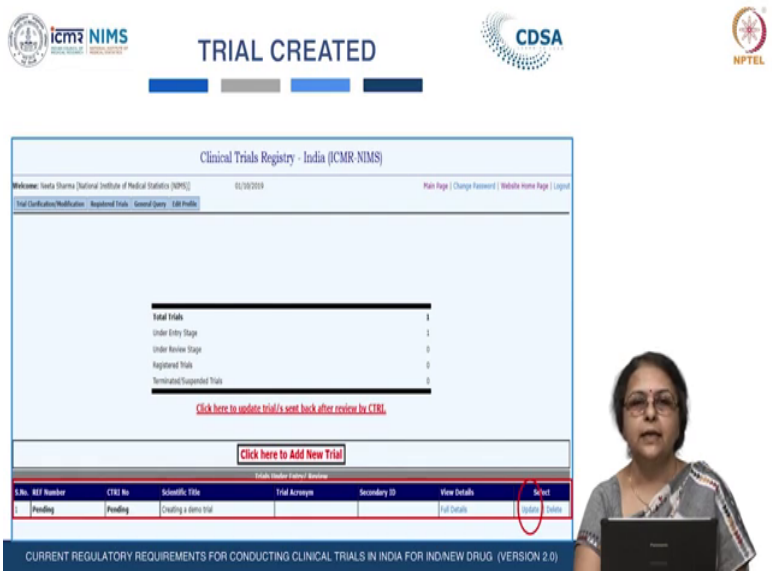
(Refer Slide Time: 11:32)

First the trial has to be created, for creation of trial the public title and the scientific title have to be provided. Acronym is an optional field, information or description of what is to be provided in each of the fields is present under this icon. Once the appropriate and necessary information has been filled click on the proceed button this would save your changes and create your trial.

(Refer Slide Time: 11:58)



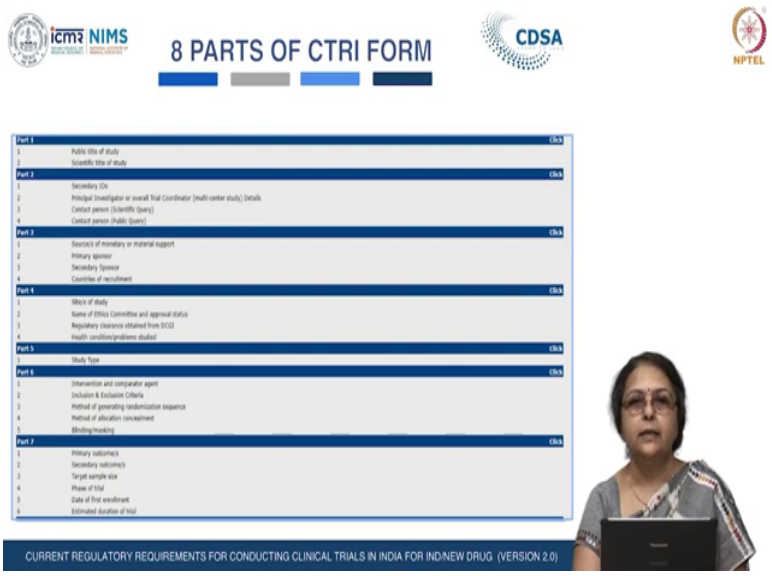
(Refer Slide Time: 12:02)



Clicking on the button will take you back to your welcome page, as you can see now your trial has been created and available under review stage. In this stage both the CTRI and the ref numbers are pending. CTRI number will be assigned only once your trial is registered, ref number will be assigned when the trial is submitted to the CTRI. Hence, at this stage the trial is not submitted to the CTRI, and hence not available to the CTRI for review or processing.

To submit your trial to the CTRI click on the update button this will display the CTRI dataset form there are eight parts to the CTRI dataset form each part may be filled individually and in any sequence.

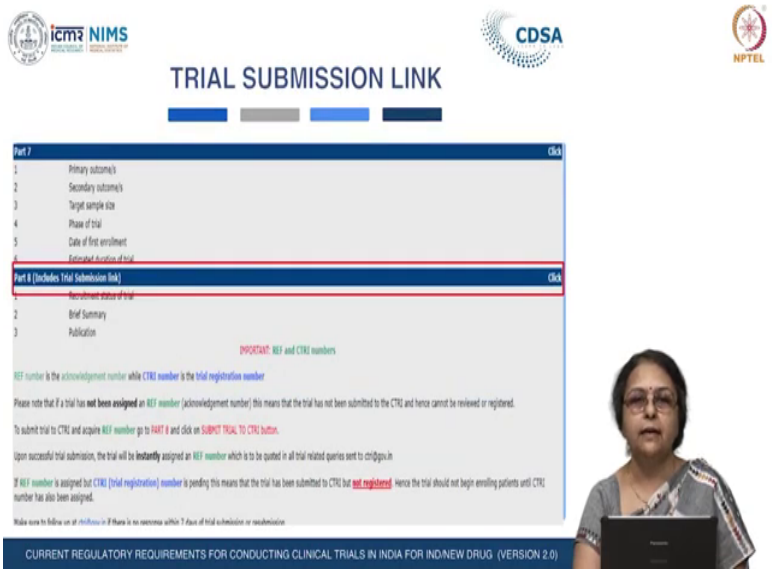
(Refer Slide Time: 12:52)



It is advisable to keep a copy of your protocol handy while filling this form. Submission of ethics approval is mandatory for registration of any clinical study in the CTRI; in addition regulatory trials must submit DCGI approval.

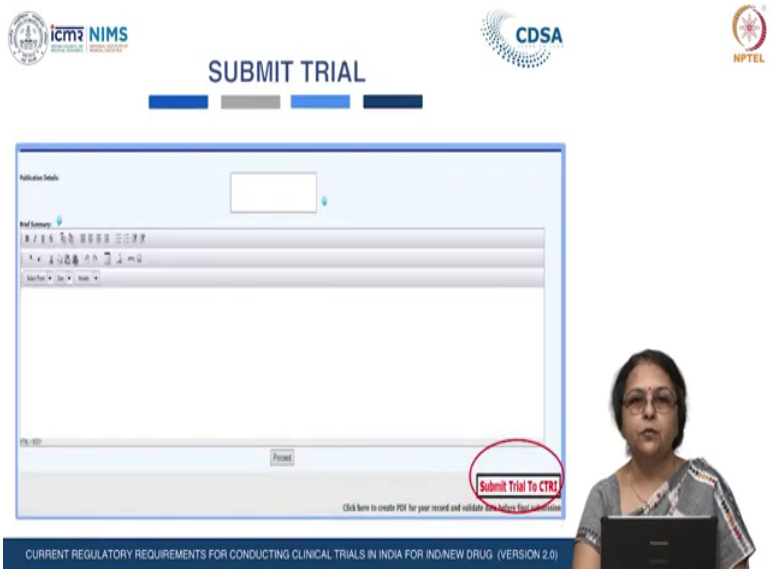
Since, the CTRI undertakes only prospective clinical trial registration that is the registration of clinical trials before the enrollment of the first patient it is advisable to submit your trial to the CTRI, well in advance of the anticipated date of first patient enrollment. To facilitate the registrant in this the CTRI encourages registrants to submit their trial for registration before receipt of ethics or DCGI approval.

(Refer Slide Time: 14:01)



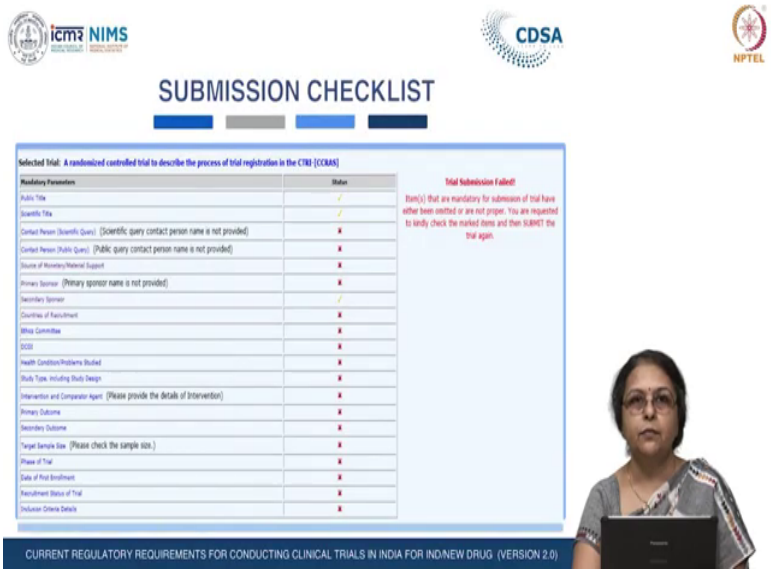
Once all the fields have been appropriately populated the trial must be submitted to the CTRI. The trial submission link is available in part eight, fill the section and click on the submit button.

(Refer Slide Time: 14:21)



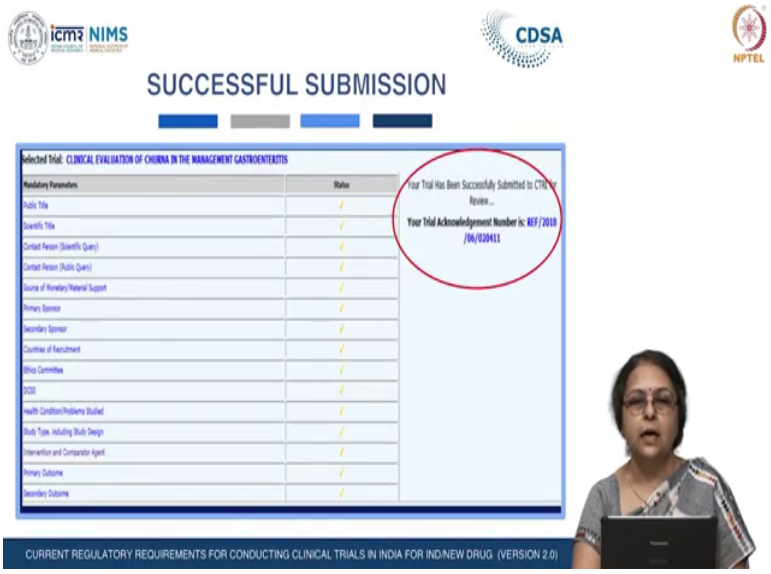
If all the fields the mandatory if all the mandatory fields have not been filled the trial will not be submitted, a cross mark will highlight the fields which need further attention. Click on the link to go back to that field and updated as applicable and try for trial resubmission submission again.

(Refer Slide Time: 14:41)



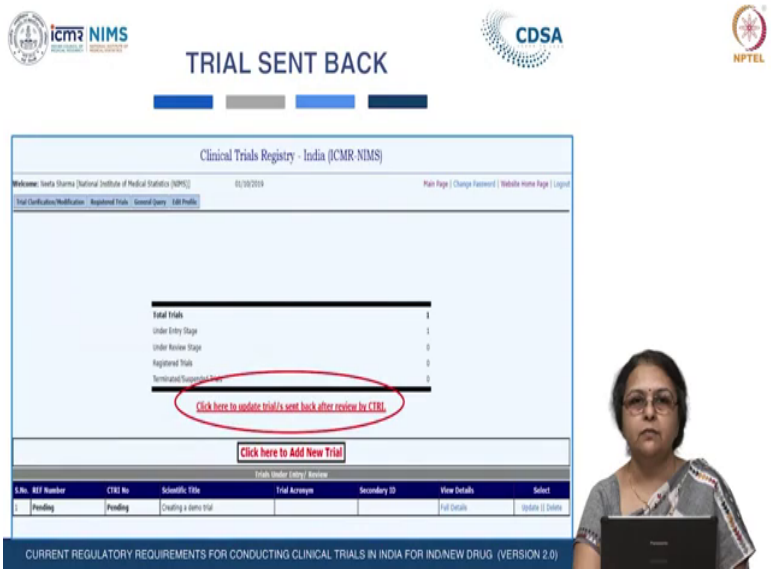
If all the fields have been filled the trial will be successfully submitted and an ref number assigned.

(Refer Slide Time: 14:50)



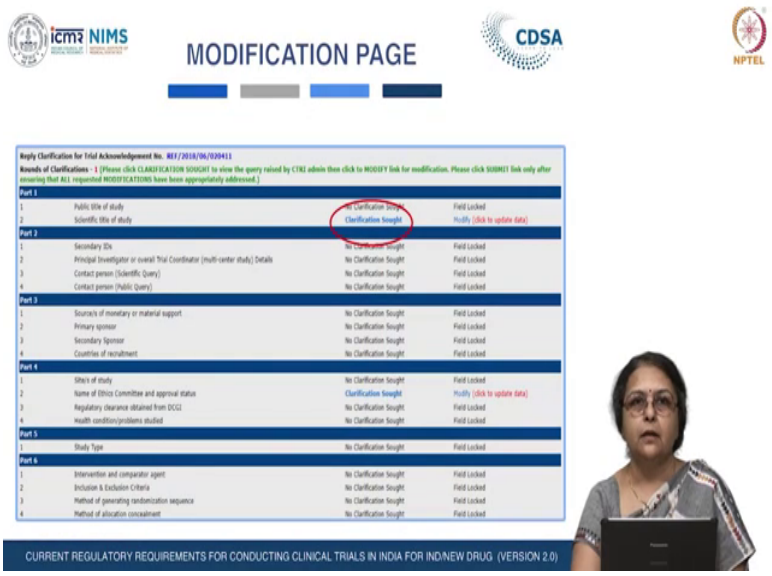
This ref number must be quoted in tall trial related queries and correspondence, once a trial has been assigned a ref number it is picked up for review by the CTRI within 7 to 10 working days.

(Refer Slide Time: 15:06)



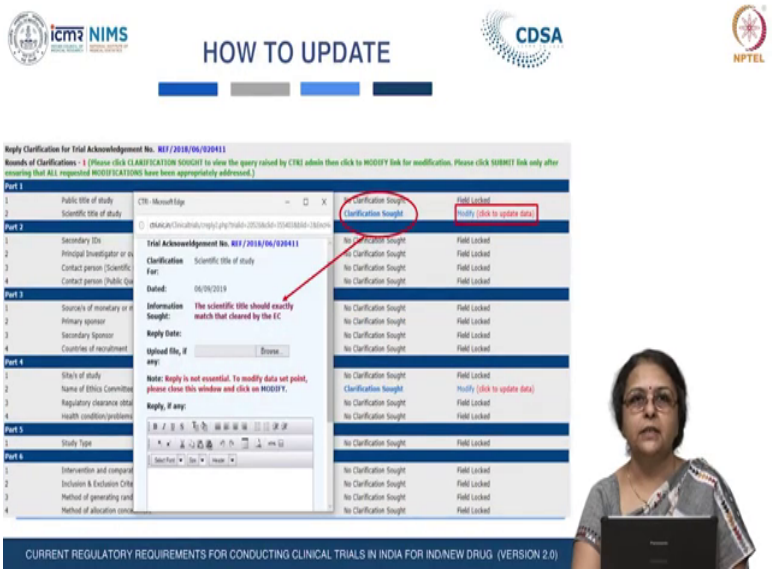
Usually the trial is sent back for modifications and clarifications and is available on the welcome page under the encircled link; in addition an automated email alert is sent to the registrant regarding the need for action on the trial.

(Refer Slide Time: 15:30)



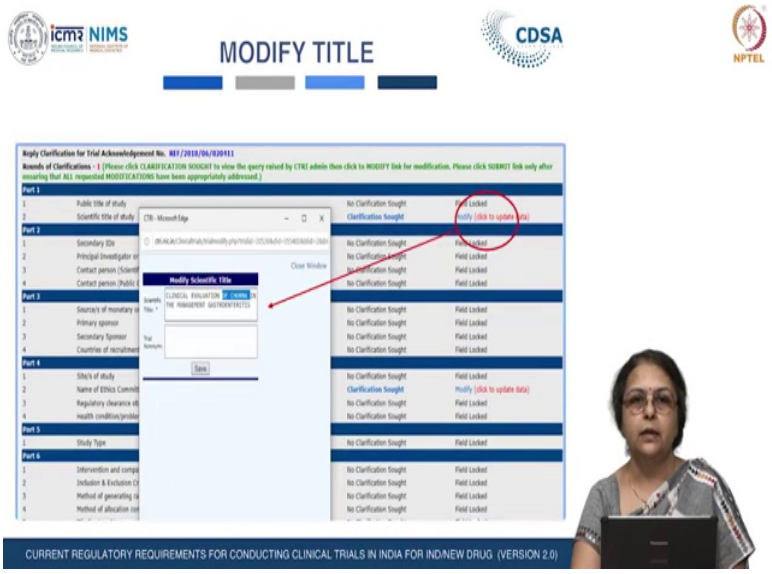
Clicking on the link will take you to the modification page, once a trial is submitted to the CTRI all fields become locked automatically only the fields which require further modifications or clarifications are unlocked.

(Refer Slide Time: 15:48)



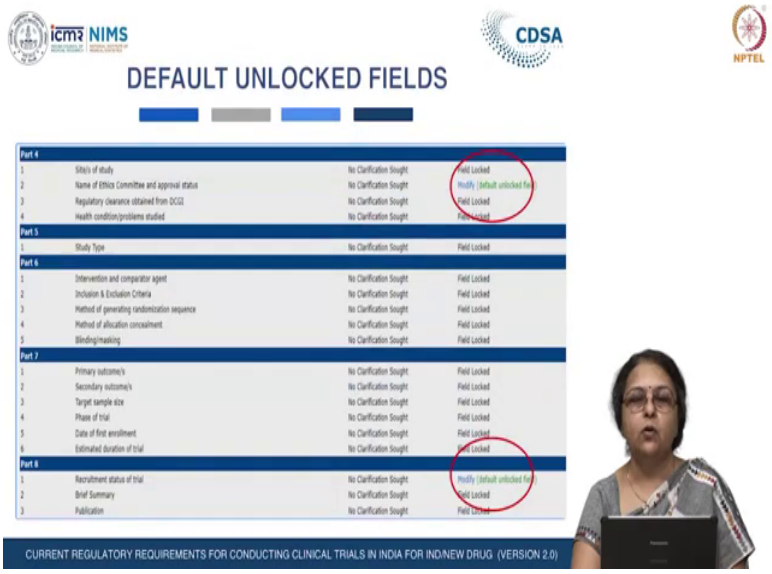
To know what clarifications are sought click on the clarification sort link this will open another window. In this case the query raised by CTRI is that the scientific title must exactly match that in the ethics approval.

(Refer Slide Time: 16:04)



In case, your ethics committee has approved a change in title you may mention the same in the reply box below and upload the relevant document in the ethics approval section. If not close this window and click on the modify link to gain access to the originally uploaded data save it and exit the field.

(Refer Slide Time: 16:28)



It may be noted that while all fields become unlocked upon submission and registration two fields that is ethics approval section and recruitment status of trial are permanently unlocked by default this is to enable regular update of the trial even upon registration. If no clarification is sought for these sections there is no need for any modifications in these fields.

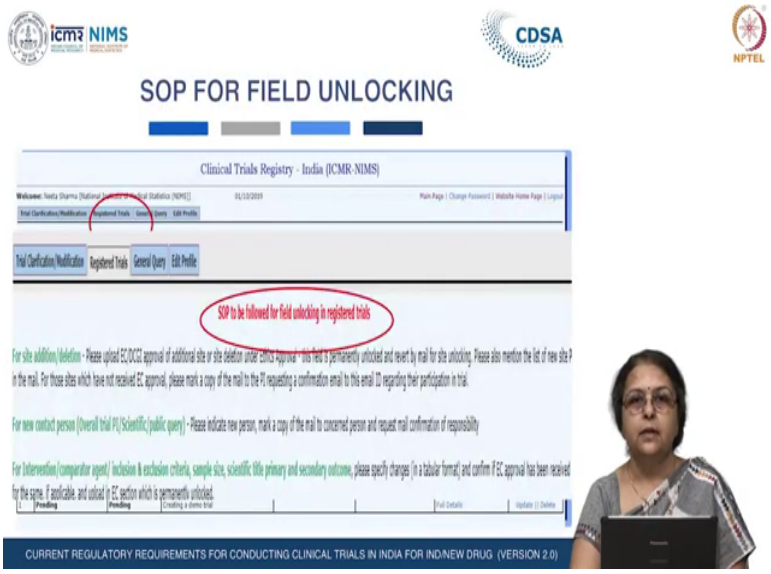
(Refer Slide Time: 16:55)

Once all the clarification sort links have been similarly addressed, make sure to submit the trial back to CTRI without this action the CTRI is not alerted on the need for action on this particular trial.

(Refer Slide Time: 17:14)

If all queries are satisfactorily addressed the trial will be registered, if not the trial will be sent back for further rounds of clarification and modification. Once registered all fields except for the default unlock fields will become locked. And after registration all trial details are expected to be regularly updated including with protocol amendments as and when applicable.

(Refer Slide Time: 17:43)



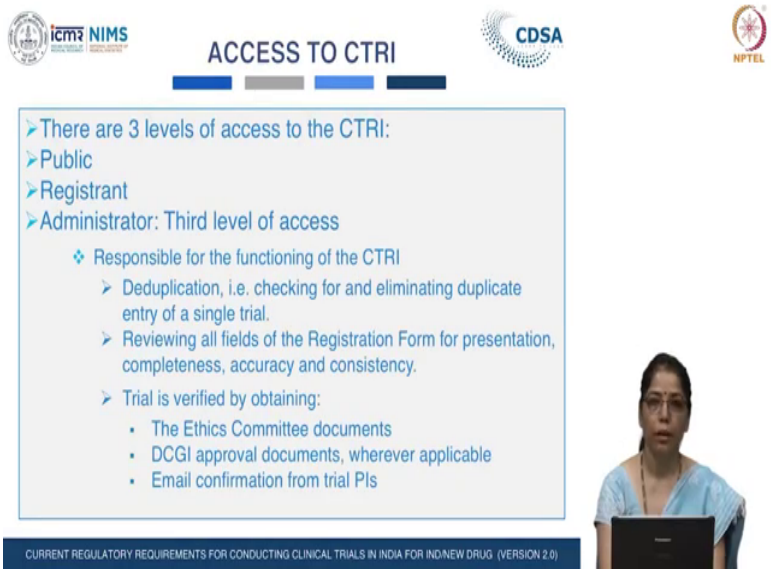
Registered trials may be viewed under this link where in case any field is required to be unlocked for updation the SOP for field unlocking is mentioned. Please, follow the same while sending along with sending a mail to the CTRI quoting the CTRI number in this subject line.

(Refer Slide Time: 18:07)

Once the trial is completed the status of trial should be changed to completed which will display two additional data set items that is data of actual study completion and final enrollment numbers achieved. In addition study results are also to be provided along with publication link if any; currently results are captured in the brief summary section.

However in the near future some structured summary results will be have to be posted in the result disclosure section which is currently being tested. In the next section Dr. Tulsi Adhikari will discuss the third and final level of CTRI access that is of the administrator, thank you.

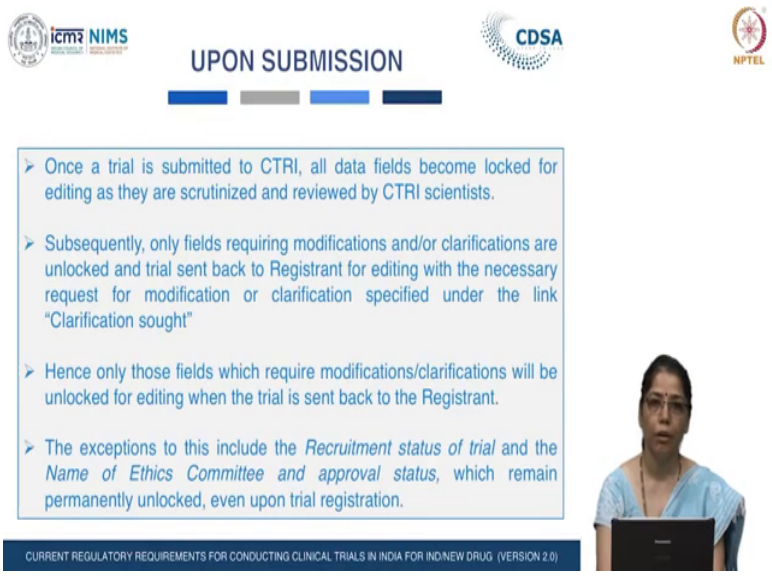
(Refer Slide Time: 18:55)



Welcome, friends I am Dr. Tulsi Adhikari and I am one of the Coordinator of CTRI and I am working as scientist e under ICMR NIMS. As my colleagues have talked about various types of accesses under the CTRI and the first one is the public access, the second one is the registrant access and the third one is the administrative access that I am talking about. So, an administrator is the identity who can make changes on the system that will affect the registering as well as the public.

And under CTRI the administrator is responsible for the duplication that is checking for an eliminating duplicate entries of a single trial also reviewing all the fields of the registration form for the trials for completeness, accuracy and consistency. And verification of the trial by obtaining; The Ethics Committee documents for that particular trial DCGI approval documents wherever applicable and email confirmation from trial principal investigators.

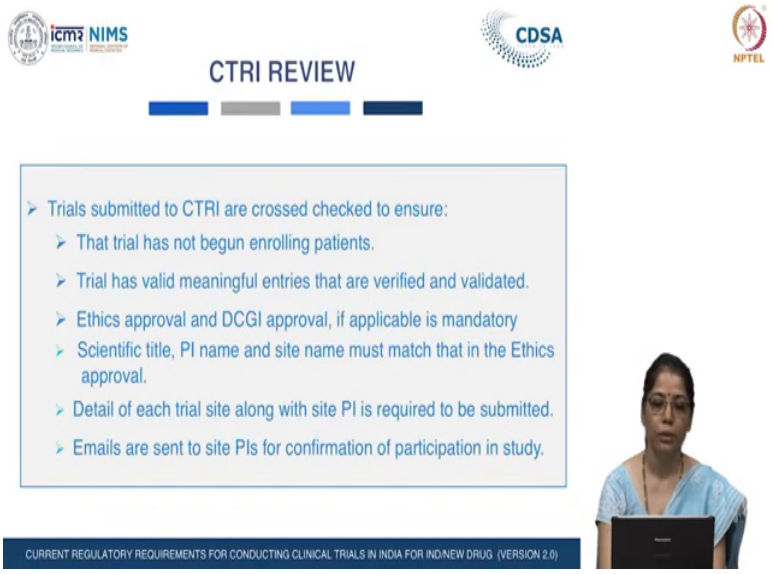
(Refer Slide Time: 20:03)



Once a trial is submitted to CTRI all data fields become unlocked for editing as they are scrutinized and reviewed by the CTRI scientist. Subsequently only fields requiring modifications and or clarifications are unlocked and the trial is sent back to the registrant for editing with the necessary request for modification or clarification specified under the link clarification sought.

Hence, only those fields which require modifications or clarifications will be unlocked for editing when the trial is sent back to the registrant. The recruitment status of the trial and Name of the Ethics Committee and approval status remains permanently unlocked even after the registration of the trial.

(Refer Slide Time: 20:51)



So, CTRI reviews all the trials submitted and trial submitted to CTRI are cross checked to ensure that trial has not begun enrolling patient that is prospective registration only. Trial has valid meaningful entries that are verified and validated ethics approval and DCGI approval if applicable is mandatory and CTRI ensures that these approvals are uploaded on the system.

Scientific title, PI name and the site name must match with that with the Ethics Committee document. Detail of each site along with the site PI is required to be submitted and emails are sent to the side PI for confirmation of participation in the study.

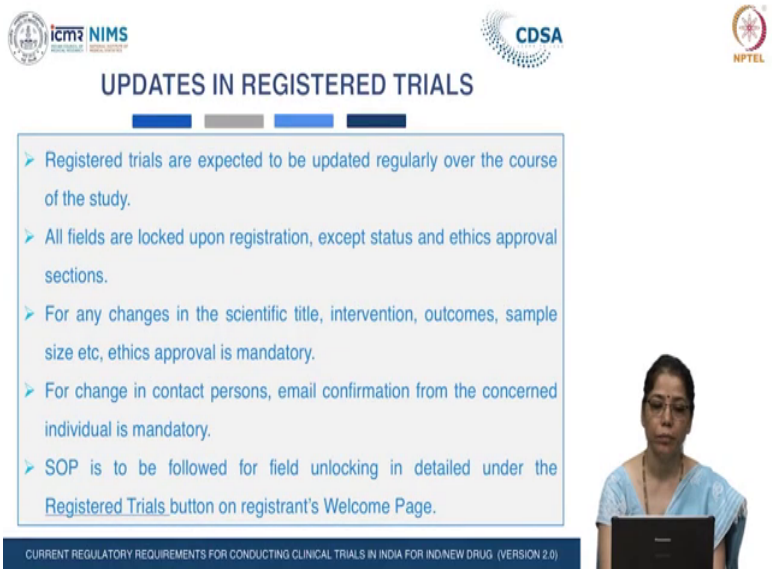
(Refer Slide Time: 21:40)

So, now I am going to give you a sample of site details what we are cover, what we all cover under the site details, the contact person name, name of the site, site address and phone number, fax and email of the contact person.

(Refer Slide Time: 21:55)

Under CTRI review the trial contact person for scientific and public queries are required to be from India only. And confirmation of participation in trial is obtained by a email from all the trial contact person other than the registering. If a trial is multi country and is registered in another registry, then the other registry number must be mentioned in secondary ID section of the CTRI form. A trial may have begun enrolling in other countries, but enrollment should not have begun in India.

(Refer Slide Time: 22:30)



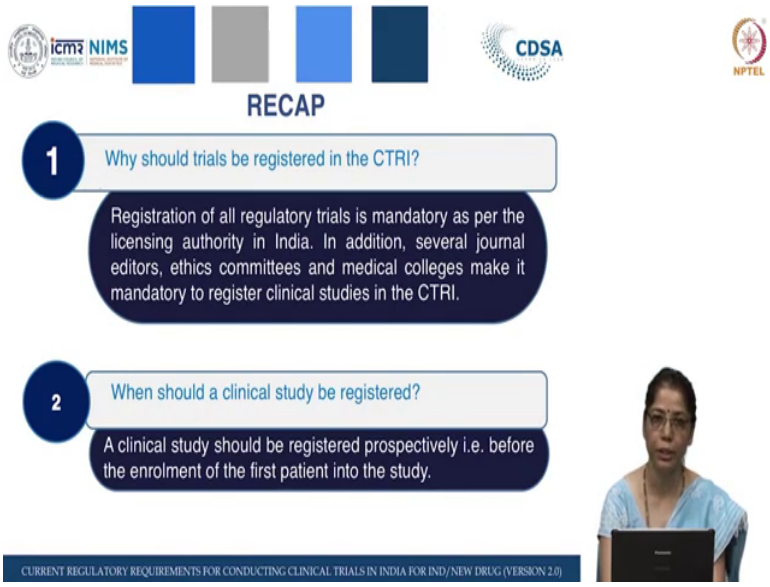
And we keep on updating the registered trials and the registered trials are expected to be updated regularly over the course of the study. All fields are logged upon registration except status and ethics approval section, for any changes in this scientific title intervention, outcome, sample size etcetera, ethics approval is mandatory. For change in contact persons email confirmation from the concerned individual is mandatory. And SOP as mentioned by Dr. Mohua is to be followed for field unlocking in detail under the registered trial button on the registrants welcome page.

(Refer Slide Time: 23:12)

That was what we are already doing in CTRI and we have plans for CTRI. So, we keep on updating the CTRI also the future plans are implement the software application for result disclosure which is currently being tested. So, we are developing the research, we are also developing the result disclosure the beta version is ready and it is being tested.

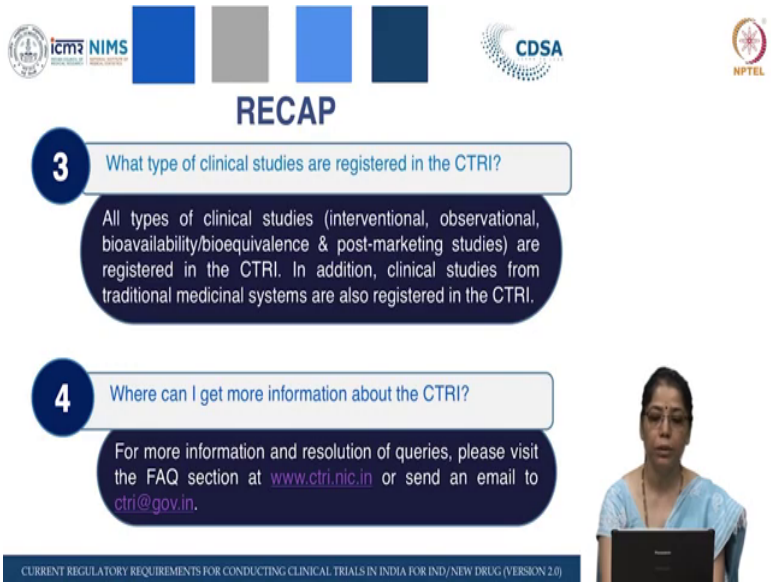
So, very soon you will see the result disclosure portal under CTRI also and we seek these stakeholder support to promote and ensure the result disclosure also. And the second future plan is develop and implement distinct data set items for Ayurveda studies also that also we have already started. So, very soon we will have a different data set items for the Ayurveda study, Ayurveda studies.

(Refer Slide Time: 24:05)



Now, let us take a quick recap what we have seen, so if we ask why should trial be registered in CTRI? The answer to this question will be registration of all regulatory trial is mandatory as per the licensing authority in India that is DCGI. In addition several journal, editors ethics committees and medical colleges make it mandatory to register clinical studies in the CTRI, when should a clinical study be registered? So, the answer to this question is a clinical study should be registered prospectively that is before the enrollment of the first patient into the study.

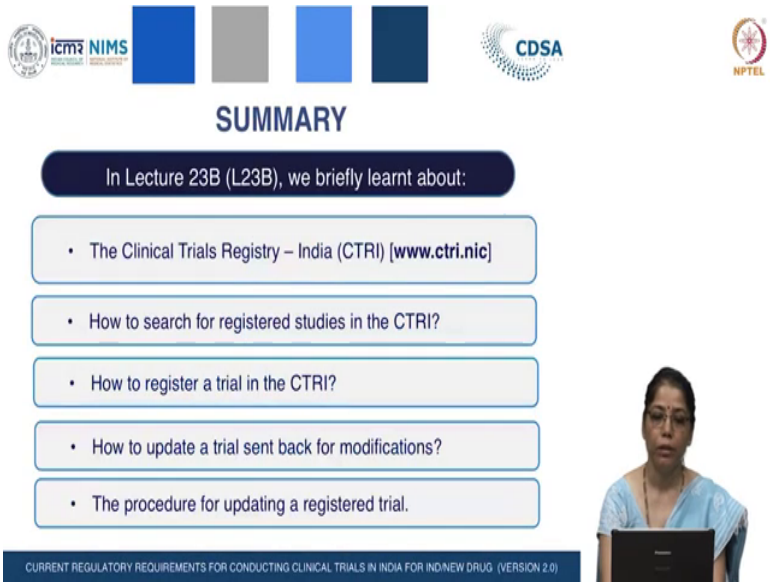
(Refer Slide Time: 24:45)



What types of clinical studies are registered in CTRI? The answer is all types of clinical studies including interventional studies, observational studies, bioavailability, bioequivalence and post marketing studies are registered in CTRI. And in addition clinical studies from the traditional system of medicines are also registered under CTRI.

And at present we have already and at present we have around 2000 Ayurveda and the and at present we have around 2000 clinical studies from the traditional system of medicine under CTRI. Where can I get more information about CTRI? So, you can have more information about CTRI under the FAQ section of CTRI and also you can send email to CTRI at this address ctri at gov dot in.

(Refer Slide Time: 25:46)



So, let us see briefly what we have learned in this lecture, the Clinical Trial Registry India is available at www dot ctri dot nic dot in. How to search for registered studies in CTRI that we have learnt? How to register a trial in CTRI? How to update a trial sent back for modification and the procedure for updating a registered trial, so all this we have learned in this lecture.

Thank you.